

A COMPREHENSIVE REVIEW OF PHYTOMOLECULES USED IN ANTI-DIABETIC ACTIVITIES

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ABSTRACT

In ancient times various medicinal plants were used for anti-diabetes as well as other disease. In such way, now many medicinal plants are subjected to show the anti-diabetes properties. The medicinal plant shows diabetes potential via activation of NF-kb, favoring pro-inflammatory cytokines, increased expression of inducible nitric oxide synthase, alpha 1 and 1 collagen, anti-oxidant activity and angiogenesis. The present review is about the treatment of anti-diabetes includes the usage of plants and the plant extract. The extracts are taken from the plants and their explants by using different solvents (water, ethanol etc..) and by using different techniques (infusion, decoction, percolation etc,..) Many studies were conducted to evaluate the extract of plants for anti-diabetes properties. Anti-diabetes process can be classified into two class, they are basic science aspect of anti-diabetes and practical aspect anti-diabetes. The basic science aspect of anti-diabetes deals with the four phases of anti- diabetes and the practical aspect anti-diabetes are subdivided into acute and chronic diabetes. This review validate the traditional claims and development of safe, effective and globally accepted medicinal plants for anti-diabetes. From this, we report various medicinal plant that can be used as anti-diabetic agent around the world.

KEYWORDS: Diabetic, Insulin, Phytomolecules, Antidiabetic.

INTRODUCTION

Diabetes mellitus is complicated metabolic/ endocrine disorder that has gravely troubled the human health and quality of life. Diabetes disease seriously threatens people’s health and is becoming more common

nowadays. Diabetes mellitus (DM) is a condition caused by high blood sugar level, inactivity, unhealthy eating, being overweight and other factors. Diabetes mellitus is clinical syndrome characterized by deficiency of insulin production or resistance to insulin action.^[1-5]

Types of Diabetes

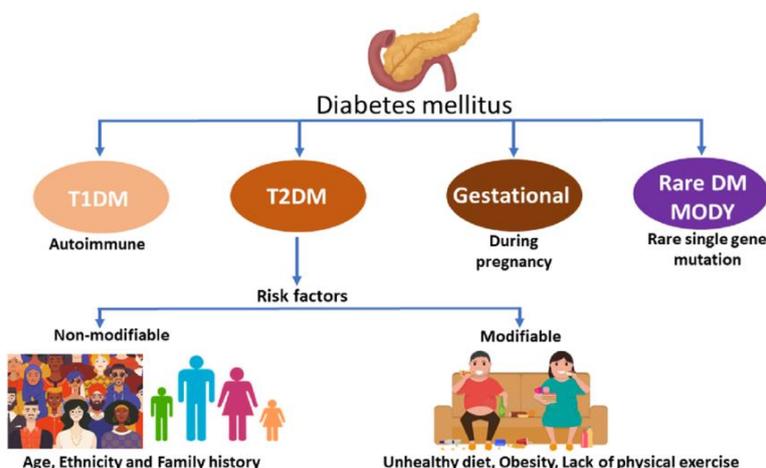


Fig. 1: Type of diabetes mellitus.

Type-1 Diabetes Mellitus

Insulin dependent diabetes mellitus (IDDM) / juvenile onset diabetes mellitus: A chronic condition in which the pancreas produce little or no insulin. There is β cell destruction in pancreatic islets; majority of cases are autoimmune (type 1A) antibodies that destroy β cells are

detectable in blood, but some are idiopathic (type 1B) - no β cell antibody is found in all type 1 cases circulating insulin levels are low or very low, and patients are more prone to ketosis. This type is less common and has a low degree genetic predisposition.

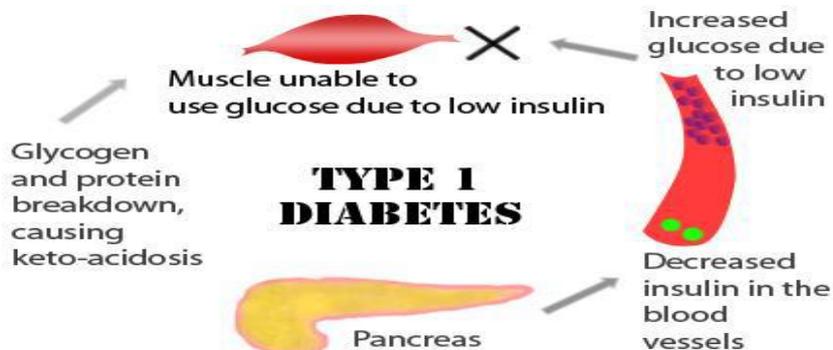


Fig. 2: Type-1 Diabetes mellitus.

Type – 2 Diabetes Mellitus

Non insulin-dependent diabetes mellitus (NIDDM) / maturity onset diabetes mellitus: There is no loss or only moderate reduction in β cell mass; insulin in circulation

is low, normal or even high, no anti- β cell antibody is demonstrated; has a high degree of genetic predisposition; generally has a late onset (past middle age). Over 90% cases of diabetes are type 2 DM.

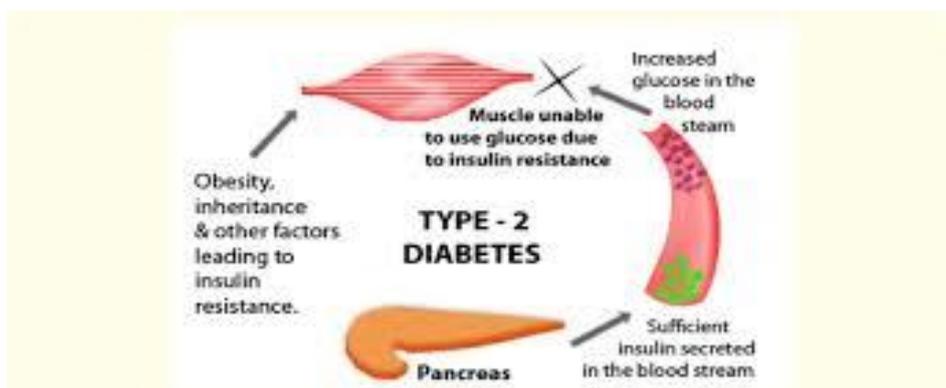


Fig. 3: Type-2 diabetes mellitus.

Gestational Diabetes Mellitus

Gestational diabetes is defined as hyperglycemia with first onset during pregnancy and is one of the common pregnancy complication. An estimated 21 million obstetric patients aged 20 to 49 years around the world are affected by GDM, and the incidence rate is up to 16.7%. The GDM is the initial normal glucose metabolism during pregnancy which affected 5 to 6% to 15 to 20% of pregnant women and 85% of live births worldwide.

of them have shown a certain degree out anti-diabetic activity by different mechanism. There various herbal anti-diabetic remedies used in various traditional system of medicine prevailing around the world 90-95% diabetes type 2.^[9]

SYMPTOMS OF DIABETES MELLITUS

Feeling more thirsty than usual, feeling very hungry, losing weight, feeling tired and weak, having blurry vision, fatigue, frequent urination, poor wound healing, yeast infections that keep coming back.

ANTI-DIABETIC

Anti diabetic is defined as the Drug that works to lower abnormally high glucose (sugar) level in the blood. All

CLASSIFICATION OF ANTIDIABETIC DRUGS

Oral antidiabetic drugs

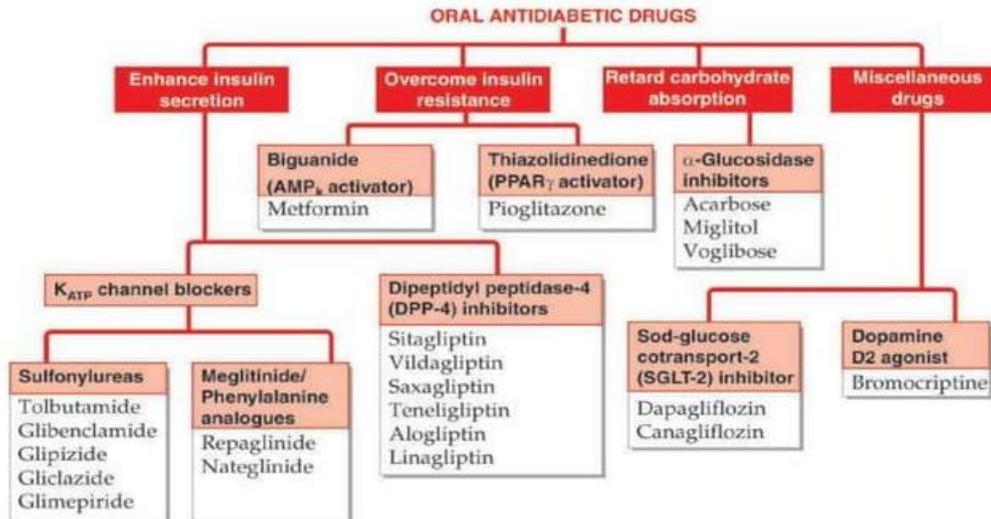


Fig. 4: Classification of anti-diabetes drugs.

SUMMARY

Class	Mechanism	Site of action	Main advantages	Main side effects
Sulfonylureas Tolbutamide Glipizide Glibenclamide (glyburide)	Stimulating insulin production by inhibiting the K _{ATP} channel	Pancreatic beta cells	• Effective • Inexpensive	• Hypoglycemia • Weight gain
Meglitinides repaglinide	Stimulates insulin secretion	Pancreatic beta cells	Sulfa free	•Hypoglycemia •Weight gain
Biguanides Metformin	Decreases insulin resistance	Liver	• mild weight loss • No hypoglycemia	• GIT symptoms, • Lactic acidosis • Metallic taste
Thiazolidinediones pioglitazone	Decreases insulin resistance	Fat, muscle		Hepatotoxicity Edema
α-Glucosidase inhibitors Acarbose	Inhibits α-glucosidase	GI tract	Low risk	•GI symptoms, flatulence
DPP-4 inhibitor Sitagliptin	Increase secretin	GI tract		

Fig. 5: Classification of anti-diabetes drugs and site of action.

INSULIN

Insulin was discovered in 1921 by willium banting and Best who demonstrated the hypoglycemic action of an extract of pancreas prepared after degeneration of the exocrine part due to ligation of pancreatic duct. It was first obtained in pure crystalline form in 1926 and the chemical structure was fully worked out in 1956 by sanger. Insulin is a peptide hormone produced by beta cells of the pancreatic islets encoded in humans by the insulin gene. It is made up of the 51 amino acids. contain 2 chain: A and B. A chain with 21 amino acid, B chain

with 30 amino acid. Insulin is a medication used in the treatment and management of diabetes mellitus type-1 and sometimes diabetes mellitus type-2, both of which are significant risk factor for coronary artery disease, strock, pheripheral vascular disease, and a host of other vascular condition.^[13]



Fig. 6: Human Insulin structure.

Insulin is a hormone that is essential for regulating energy storage and glucose metabolism in the body. Insulin in liver, muscle, and fat tissues stimulated the cell

to take up glucose from blood and store it glycogen in liver and muscle. The failure of insulin control causes diabetes mellitus.

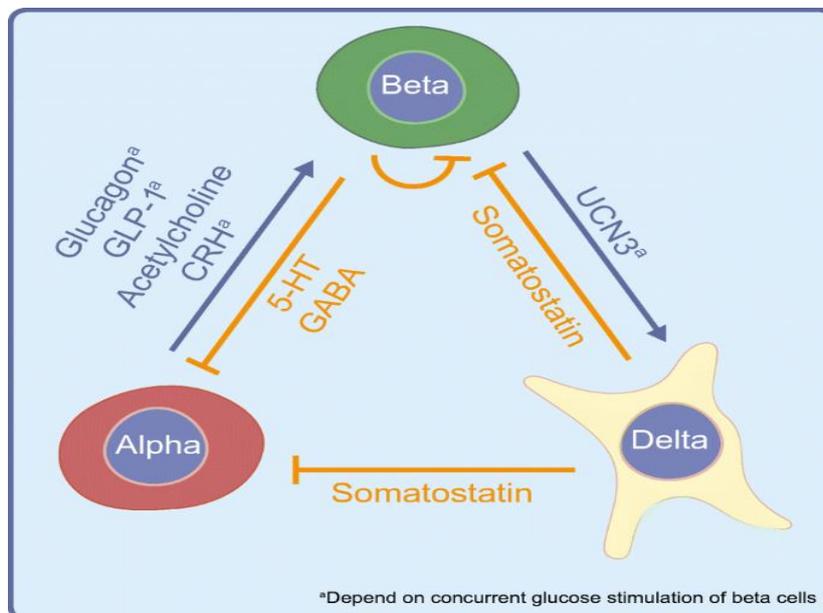


Fig. 7: Paracrine modulation of hormone secretion within the pancreatic islets of Langerhans.

CONTROL DIABETES IN WITHOUT MEDICINE

Diabetes is a serious health condition that occurs due to high blood sugar. there are several way to control diabetes naturally. Diabetes is one of main causes of several heart diseases, kidney disease, eye diseases, strock, skin problems, and many other health problems. control the diabetes mellitus is following steps.

- 1) Exercise regularly
- 2) Manage your carbohydrate intake
- 3) Consume more fiber
- 4) Drink plenty of water and stay hydrated
- 5) Implement portion control in food
- 6) Choose foods with a low glycemic index
- 7) Try to manage your stress level
- 8) Monitor your blood sugar levels
- 9) Get enough quality sleep

- 10) Eat foods rich in chromium and megnesium
- 11) Consider adding specific foods to your diet
- 12) Maintains a moderate weight
- 13) Eat healthy snacks more frequently
- 14) Eat probiotic-rich foods.

Exercise Regularly

Regular exercise can help you reach and maintain a moderate weight and increase insulin sensitivity. Increase insulin sensitivity means your cells can more effectively use the available sugar in your bloodstream. Exercise also helps your muscles use blood sugar for energy and muscle contraction.

Manage Your Carbohydrate Intake

Your body breaks carbohydrate down into sugars, mainly glucose. Then, insulin helps your body use and store it for energy. The eating a low carbohydrate diet helps reduce blood sugar levels and prevent blood sugar spikes.

Eat More Fiber

Fiber slows carbohydrate digestion and sugar absorption, thereby promoting a more gradual rise in blood sugar levels. There are two types of fiber-insoluble and soluble.

Foods that are high in fiber include:

- Vegetables
- Fruits
- Legumes
- Whole grains

Drink Water and Stay Hydrated

Drinking enough water could help you keep your blood sugar levels within healthy ranges. In addition to preventing dehydration, it helps your kidney flush out any excess sugar through urine. Drinking water regularly may rehydrate the blood, lower blood sugar levels, and reduce diabetes risk.

Implement Portion Control

Portion control can help you regulate your calorie intake and maintain a moderate weight. Consequently, weight management promotes healthy blood sugar levels and has been shown to reduce the risk of developing type 2 diabetes.

Choose Foods With A Low Glycemic Index

The glycemic index divides foods into low, medium, and high GI and ranks them on a scale of 0-100. Low GI foods have a ranking of 55 or less. Both the amount and type of carbohydrate you eat determine how a food affects your blood sugar levels. Specifically, eating low GI foods has been shown to reduce blood sugar levels in people with diabetes.

Try To Manage Your Stress Levels

Stress can affect your blood sugar level. One study including a group of students showed that exercise, relaxation, and meditation significantly reduced stress and lowered blood sugar levels.

Monitor Your Blood Sugar Levels

Monitoring blood glucose levels can help you better manage them. Try measuring your levels regularly every day and keeping track of the numbers in a log. Also, it may be more helpful to track your blood sugar in pairs—for example, before and after exercise or before and 2 hours after a meal.

Get Enough Quality Sleep

Getting enough sleep feels excellent and is necessary for good health. Adequate sleep is about both quantity and

quality. The National Sleep Foundation recommends that adult get at least 7-8 hours of high quality sleep per night.

Eat Foods Rich In Chromium And Magnesium

High blood sugar levels and diabetes have been linked to micronutrient deficiencies. Some examples include deficiencies in the minerals chromium and magnesium. Chromium is involved in carb and fat metabolism. It may potentiate the action of insulin, thus aiding blood sugar regulation.

Chromium- rich foods

- Meats
- Whole grain products
- Fruit
- Vegetables
- Nuts

Magnesium-rich foods

- Dark leafy greens
- Tuna fish
- Bananas
- Beans
- Avocados
- Whole grains

Consider Addind Specific Foods To Your Diet

Multiple foods and plants are known to have medicinal properties. Some of the foods touted to have anti-diabetes effect include:

- Apple cider vinegar this ingredient may reduce blood sugar levels by delaying the emptying of your stomach after a meal.
- Fenugreek seeds there is some evidence that fenugreek may help support blood sugar management.

Maintain A Moderate Weight

Maintaining a moderate weight promotes healthy blood sugar levels and reduces your risk of developing diabetes. Research shows that even a 5% reduction in body weight can improve your blood sugar regulation and reduce the need for diabetes medication.

Eat Healthy Snacks More Frequently

Snacking between meals may also reduce your risk of the type 2 diabetes. Spreading your meals and snacks throughout the day may help you avoid both high and low blood sugar levels.

Eat Probiotics-Rich Foods

Probiotics are friendly bacteria that offer numerous health benefits, including improved blood sugar regulation.

FORMULATED PHYTOMOLECULES FOR ANTI-DIABETIC ACTIVITIES

Many phytomolecules which are obtained from the

medicinal plants have been reported to show the anti-diabetic activity. These phytochemicals are obtained from the medicinal plants and their explants by extraction process. The whole part of medicinal plant contain a many phytochemicals which has many uses. These medicinal plants synthesize many chemical compounds for various function such as defense and protection against microorganism, insects, and also for many diseases.

1. FENUGREEK

Name: Fenugreek.

Scientific name: *Trigonella foenum graecum*.

Family: *Fabaceae*

Phytochemicals: Alkaloids, Flavonoids.

Source: Seeds



Fig. 8: Fenugreek.

Description

The conclusion of the present study indicates some promising properties for fenugreek seeds on biomarkers of inflammation and oxidative stress in T2 DM patients. FS intake has some beneficial effects on FPG, SBP, and liver and kidney function in T2 DM patient.

2. BITTER MELON

Name: Bitter melon.

Scientific name: *Momordica charantia*

Family: *Cucurbitaceae*.

Phytochemicals: Saponins, tannins.

Source: fruit.



Fig. 9: Bitter Melon.

Description

Bitter melon has potential anti-diabetic effects in humans. Thus bitter melon may be a useful option as adjuvant treatment in patients with type 2 diabetes. It is

possible that this herb is beneficial not only on glycemic complication of type 2 diabetes.

3. NEEM

Name: Neem.

Scientific name: *Azadirachta indica*.

Family: *Meliaceae*

Phytochemicals: Alkaloids, flavonoids, phenol.

Source: leaves



Fig. 10: Neem.

Description

The conclusion of the neem extract helps of the increase overall the insulin levels.

4. SHAMEPLANT

Name: Shameplant.

Scientific name: *Mimosa pudica*.

Family: *Fabaceae*.

Phytochemicals: Amino acid and protein, tannins.

Source: Whole plant



Fig. 11: Shameplant

Description

The phytoconstituents in the extracts also improved glutathione levels, possibly modulating GSH-biosynthesis. Hence, it is clear that the *M.pudica* can be leading source of anti-diabetic drug candidate, which equally modulate the secondary diabetic complication.

5. GREEN CHIRETTA

Name: Green chiretta.

Scientific name: *Andrographis paniculata*.

Family: *Acanthaceae*

Phytochemicals: Terpenoids and Saponins..

Source: leaves



Fig. 12: Green chiretta.

Description

Future perspective for andrographolide as an anti-inflammatory agent.

6. JAVA PLUM

Name: Jamun plum.

Scientific name: *syzygium cumini*.

Family: *Myrtaceae*.

Phytomolecules: Gallic acid and Quercetin.

Source: seeds



Fig. 13: Jamun plum.

Description

Studies have shown that various extracts of jamun possess a range of pharmacological actions such as the anti-inflammatory, anti-ulcerogenic, anti-cancer, antiallergic and anti-diabetic effects supporting its traditional use.^[8,16]

7. INDIAN BAEL

Name: Indian bael.

Scientific name: *Aegle marmelos*.

Family: *Rutaceae*.

Phytomolecules: Carotenoids and phenolic compound.

Source: Fruit.



Fig. 14: Indian bael.

Description

Among the various life style approaches for the management of this disease dietary intervention with a

vegetarian diet seems to be an economical physiological and safe approach for the prevention and possible management of T2 DM.

8. ALEO VERA

Name: Aleo vera.

Scientific name: *Aleo vera*.

Family: *liliaceae*

Phytomolecules: Anthraquilones and falvonoids.

Source: leaves.



Fig. 15: Aleo vera.

Description

The result suggest that fraction D and subfraction D1 from aqueous extracts of Aleo vera leaf possesses the maximum FSH lowering capacity and further investigation is required for determination of anti-diabetic principal(s) and exact mechanisms of their hypoglycemic action.

9. GUAR

Name: Guar.

Scientific name: *cyamopsis tetragonoloba*.

Family: *Fabaceae*.

Phytomolecules: Caffeic acid and gallic acid.

Source: Seeds.



Fig. 16: Guar.

Description

C. tetragonoloba beans also protected β -cell mass and lessened hyperlipidemia in insulin resistant animal model. Hence this can be considered for use in the management of T2DM.

10. GURMAR

Name: Gurmar.

Scientific name: *Gymnema sylvestre*.

Family: *Asclepiadaceae*.

Phytomolecules: Gymnemic acid and lupeol.

Source: leaves (or) root



Fig. 17: Gurmar.

Description

The results suggest that the polyherbal formulation GSPF may have the potential to regulate both hyperglycemia and possibly hyperlipidemia." GSPF kwath" may be a potential safe and effective therapy for the treatment of the type 2 diabetes mellitus.

11. CURRY LEAVES

Name: Curry leaves.

Scientific name: *Murraya koenigii*

Family: *Rutaceae*

Phytomolecules: phenolic and carbozole alkaloids.

Source: Leaves



Fig. 18: Curry leaves.

Description

The result of our study scientifically support the traditional belief for using the leaves *Murraya koenigii* as adjuvant, in the treatment of pain disorders related to renal impairments among diabetes.

12. INDIAN GOOSEBERRY

Name: Indian gooseberry.

Scientific name: *Phyllanthus wmblica*.

Family: *dhyllanthaceae*.

Phytomolecules: Gallic acid and ellagic acid.

Source: Fruit.



Fig. 19: Indian gooseberry.

Description

In conclusion, we found that the IGBP mixture inhibits adipogenesis and lipogenesis and promotes lipolysis, thereby regulating energy metabolism in C57BL/6J mice with HFD- induced obesity. There fore, it will be

proposed that the dietary mixture of IGBP helps to reduce the body fat. Our finding also suggest that the mixture may potentially exert anti-diabetes affects by reducing blood glucose, insulin, and HbAlc level in animal.

13. GARLIC

Name: Garlic

Scientific name: *Allium sativum*.

Family: *Amaryllidaceae*.

Phytomolecules: Ajoene and falvonoids.

Source: Raw garlic extract



Fig. 20: Garlic.

Description

It is concluded that the plant must be considered as excellent candidate for future studies on diabetes mellitus.

14. SUGAR APPLE

Name: Sugar apple.

Scientific name: *Annona squamosa*.

Family: *Annonaceae*.

Phytomolecules: Alkaloids or falvonoids.

Source: Fruit



Fig. 21: Sugar apple.

Description

It acts by promoting insulin release from the pancreatic islets, increasing utilization of glucose in muscle and inhibiting the glucose output from liver.

15. PERIWINKLE

Name: Periwinkle.

Scientific name: *Vinca*.

Family: *Apocynaceae*.

Phytomolecules: Vinblastine and vincristine.

Source: Methanolic vinca rosea extracts.



Fig. 22: Periwinkle.

Description

The methanolic whole plant extract at high dose (500mg/kg) exhibited significant anti-hyperglycemia activity than whole plant extract at low dose (300mg/kg) in diabetic rats.

16. TURMERIC

Name: Turmeric.

Scientific name: *Curcuma longa*.

Family: *Zingiberaceae*.

Phytomolecules: protein and demethoxycurcumin.

Source: Turmeric powder or extract.



Fig. 23: Turmeric.

Description

Turmeric extracts demonstrated an anti-diabetic effect in streptozotocin. Nicotinamide induced type 2 diabetic wistar rats.

17. TANNERS CASSIA

Name: Tanners cassia.

Scientific name: *Senna auriculata*.

Family: *Fabaceae*.

Phytomolecules: Alkaloids and tannins flavonoids.

Source: leaves and flowers.



Fig. 24: Tanners cassia.

Description

It is concluded that alkaloids and flavonoids present in the acetone extract of senna auriculata flower may be responsible for the activity.

18. PUNARNAVA

Name: punarnava.

Scientific name: *Boerhavia diffusa*.

Family: *Nyctaginaceae*

Phytomolecules: Alkaloids and flavonoids, steroids.

Source: Leaves.



Fig. 25: Punarnava.

Description

The chloroform extract of the leaves of punarnava can reduce blood glucose level and shows a significant increase in plasma insulin levels.

19. WHITE MULBERRY

Name: White mulberry.

Scientific name: *Morus alba*.

Family: *Moraceae*.

Phytomolecules: Gallic acid and caffeic acid, rutin.

Source: Fruit.



Fig. 26: White mulberry.

Description

In addition to lowering blood glucose levels, many animal studies observed white mulberry extract decreased oxidative stress and typically vulnerable to diabetic complications.

20. OCIMUM SANCTUM

Name: Holy basil.

Scientific name: *Ocimum tenuiflorum*.

Family: *Lamiaceae*.

Phytomolecules: Eugenol, rosmarinic acid.

Source: Leaves and extract.



Fig. 27: Ocimum sanctum.

Description

Ocimum sanctum leaves have been traditionally used in treatment of diabetes mellitus. Dietary supplementation of fresh tulsi leaves in a dose of 2 gm/kg BW for 30 days led to significant lowering of blood glucose levels in test group.

21. SWEET POTATO

Name: Sweet potato.

Scientific name: *Lpomoea batata*.

Family: *Convolvulaceae*.

Phytomolecules: Flavonoid and anthocyanins.

Source: Tubers.



Fig. 28: Sweet potato.

Description

Sweet potatoes that have the potential to be anti-diabetic include white, purple, orange, and Japanese green sweet potatoes. Phenolic acids, flavonols, flavanones, and anthocyanidins are responsible for the anti-diabetic activity of sweet potatoes. The anti-diabetic mechanism of sweet potatoes is determined by a combination of components with multi- target action.

22. LOTUS

Name: Lotus.

Scientific name: *Nelumbo nucifera*.

Family: *Nelumbonaceae*.

Phytomolecules: Troanthocyanidins and terpenoids.

Source: flower.



Fig. 29: Lotus.

Description

The ethanolic extract of both flowering aquatic plants shows potent antioxidant and anti-diabetic activities. Thus, flowering parts of both aquatic plants can be good source of herbal medicine for diabetes and problems associated with free radicals.

23. SACRED FIG

Name: Sacred fig.

Scientific name: *Ficus religiosa*.

Family: *Moraceae*.

Phytomolecules: Genticic acid.

Source: Whole plants.



Fig. 30: Sacred fig.

Description

From this study, we can conclude that aqueous extract of ficus religiosa bark has beneficial effects on bloods glucose level. It has the potential to impart therapeutic effect in diabetes.

24. MINT BUSH

Name: Mint bush.

Scientific name: *Prostanthera*.

Family: *Lamiaceae*.

Phytomolecules: Flavonoids and terpenoids.

Source: Leaves.



Fig. 31: Prostanthera.

Description

The study shows that crude extract of *L. ovalifolia*. The activity of anti-glycation of advanced glycated end product (AGHs) as well as GLUT4 translocation.

25. MORINGA

Name: Moringa.

Scientific name: *moringa oleifera*.

Family: *moringaceae*.

Phytomolecules: Rutin and kaempferol.

Source: Leaves.



Fig. 32: Moringa.

Description

They have been shown to have insulin-resistant anti-diabetic activity.

26. BITTER LEAF

Name: Bitter leaf.

Scientific name: *Vernonia amygdalina*.

Family: *Asteraceae*.

Phytomolecules: Phenolic acid and xanthones.

Source: leaves.



Fig. 33: Bitter leaf.

Description

The various medicinal plants have been reported to exhibit anti-diabetic properties and VA in the no exception. The VA has demonstrated hypoglycemic abilities.

27. DOUM PALM

Name: Doum palm.

Scientific name: *Hyphaene thebaica*.

Family: *Arecaceae*.

Phytomolecules: Phytoene and liriiodenine xanthophylls.

Source: Fruits



Fig. 34: Doum palm.

Description

The result of the use of WF and compound the epicarp as anti-diabetic agent, taking into consideration.^[1]

28. AVOCADO

Name: Avocado.

Scientific name: *Persea Americana*.

Family: *Lauraceae*.

Phytomolecules: Hydroxybenzoic acid.

Source: Leaves.



Fig. 35: Avocado.

Description

The result indicates that the hydroalcoholic extract of the leaves of *Persea Americana* has anti-diabetic properties and possibly acts to regulate glucose uptake in liver and muscles by way of PKB/AKT activation restoring to intracellular energy balance.

29. OLIVE

Name: Olive.

Scientific name: *Olea europaea*.

Family: *Oleaceae*.

Phytomolecules: Benzoic acid and cinnamic acid.

Source: leaves.



Fig. 36: Olive.

Description

The use of olive leaf extracts alone (or) as an adjuvant agent with treatment protocol of diabetes mellitus type -2 at the dose of 200 mg once a day.^[4]

30. OKRA

Name: Okra.

Scientific name: *Abelmoschus esculentus*.

Family: *Malvaceae*

Phytomolecules: Polyphenols and flavonoids.

Source: ladies finger.



Fig. 37: Okra.

Description

This study is the first meta-analysis to evaluate the effect of okra on glycaemic control in pro-diabetic and T2D patient. The direct beneficial effect of okra as an anti-hyperglycemic remedy has been demonstrated.

CONCLUSION

There are several herbal medicinal plant in this world which contain many phytomolecules it deal with number of diseases and resolved. These medicinal plants are used traditionally and also by tribal people. The extract of plant was obtained by the extraction method such as soxhlets, percolation, maceration, decoction and etc,.. From the extract some formulations such as ointment, gel, nanoemulsion and others was formulated and evaluated. Many medicinal plants are proven to show the anti-diabetes activities from that we had investigate about some plants such as fenugreek, bitter melon, neem, shameplant, green chiretta, java plum, Indian bael, aloe vera, guar, gurmar, curry leaves, Indian gooseberry, garlic, sugar apple, periwinkle, turmeric, tanners cassia, punarnava, white mulberry, ocimum, sweet potato, lotus, sacred fig, mint bush, moringa, bitter leaves, doum plam, avocado, olive and okra. The goal of our review work is to study about these plants and their phytomolecules and also their activities on several diabetes. The results that we had studies from the below references are reported in our review work.

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