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REVIEW ARTICLE

Antidiabetic Potential of Ethnomedicinal Plants of Western Ghats, India: A Review

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ABSTRACT

Diabetes mellitus is a chronic hyperglycemic condition resulting from defects in insulin secretion, insulin action. The uncontrolled and chronic hyperglycemia will lead diabetic complications, subsequent protein glycosylation, coagulation defects, hypoxia, and ischemia. The current therapy diabetes mellitus (DM) is only to control the blood glucose and unable to monitor, mitigate and reduce the complications associated with the DM. They also have many adverse effects, and many patients need monitoring and management for long term complications. The Ayurveda system found many herbs which exhibit promising results pre-clinically, clinically in the management of DM and beneficial effects in DM complications. Recently, herbal medicines are gaining importance in the management of DM. This article attempts to provide information about medicinal plants of Western Ghats, India was used for the management of DM and its complications.

KEYWORDS

Diabetes mellitus, Western Ghats plants, Secondary metabolites

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders - defects in insulin secretion, or insulin action. The chronic diabetes mellitus (DM) and uncontrolled diabetes lead to many diabetic complications such as diabetic cardiomyopathy, nephropathy, neuropathy, etc. In 2011, 366 million people were suffered from DM in 2011 and may increase to 552 million by 2030.[1-2] The present review deals with some selected western ghat medicinal plants, their secondary metabolites and their beneficial effects in DM and its complications.[3-7]

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The various phytoconstituents possess many pharmacological effects by different mechanisms and help to control the diabetic complications were shown in Table 1. The secondary metabolites structures possessing antidiabetic effects were illustrated in figure 1.

1. *Aegle marmelos* (L)Corr. Ex. Roxb (Rutaceae)

The bael fruit reported maintaining hypoglycemic activity more significant than standard glibenclamide in diabetic rats. The hypoglycemic effect is due to the presence of coumarins in fruit, which promotes insulin secretion. The bael fruit, leaves, and seeds have shown a significant hypolipidemic effect in diabetic rats. The pretreatment of bael leaf at 100 mg/kg and 200 mg/kg for 35 days reported marked improvement in a decrement of lipid peroxides, plasma lipids, and lipoproteins and suggesting its antihyperlipidaemic effect.

Table 1: Various antidiabetic mechanisms of Ethnomedicinal plants of Western Ghats of India

Sl. No.	Medicinal plants	Anti-diabetic mechanisms of action	Ref
1	*Aeglemarmelos*(L.) Correa Ex Roxb. (Rutaceae), Leaves, Stem bark, Fruits	α-glucosidase inhibition Insulin secretogauge Inhibit the lens aldose reductase, Antiglycating Enhances PPAR-γ expression Regeneration of β cells	13 14 17 18
2	*Aloe Barbdensis* mill (Alliaceae) Leaf	α-glucosidase inhibition Inhibits glycogen synthase kinase-3β Up-regulation of GLUT-4 mRNA synthesis and PPARα expressions Increase the β-oxidation enzymes (ACO, CPT1)	20 21 22 23
3	*Andrographispaniculata*(Burm.f.) Wall. (Acanthaceae)	Inhibition of *α*-glycosidase and *α*-amylase Enhances GLUT4 translocation Reduces oxidative free radical generation	 28 29
4	*Azadirachtaindica*A. Juss.(Meliaceae) Leaves, Seed	Inhibition of α-glucosidase& α-amylase Inhibit intestinal maltase, glucoamylase, sucrose-isomerase, lactase, trehalase enzymes Reduces the oxidative stress & AGE formation	31 32 33
5	*Buteamonosperma* (Fabaceae) Leaves, bark, flowers, and seeds	Enhances insulin secretion and glycogen formation Reduces hepatic G-6Pase Reduces oxidative-stress	35 36 37-38
6	*Casearіaesculenta*Roxb. (Flacourtiaceae) Root	-	39-43
7	*Catharanthusroseus*(L.) G. Don Apocynaceae) Leaves	Increases glucose-stimulated insulin secretion Protect β-cells from the cytokines-induced apoptosis Inhibition of Protein tyrosine phosphatase-1B (PTP-1B) inhibition activity	 44 45

Table 1: Countinue……..

8	*Cinnamomumzeylanicum*Blume (Lauraceae) Bark	Delays gastric emptying Inhibits pancreatic amylase Inhibition of glucosidase Enhances insulin receptor phosphorylation Increases GLUT 4 synthesis membrane translocation	46-47
9	*Curcuma longa* L. (Zingiberaceae) Rhizome	β-cell regeneration, TNF-α, FFA, NF-κB, TBRS, PPAR-γ & Nrf2	50-51
10	*Ficus racemosa* Linn (Moraceae) Fruit, stem bark	Inhibition of α-glucosidase & α-amylase	52-54
11	*Gymnema sylvestre* (Asclepiadaceae) Leaves, stem	Regeneration of β-cells and increases β-cells Attenuation of the insulinotropic action of gastrointestinal hormones	56-59
12	*Melia azedarach* L (Meliaceae) Leaves, fruits	Inhibition of PTP-1B	61-64
13	*Ocimum sanctum* L. (Lamiaceae) Leaves, seed	Enhances insulin secretion Reduces oxidative stress	65
14	*Pongamia pinnata* (Linn.) Pierre (Leguminosae) Leaves, stem bark & fruits	Enhances translocation of GLUT4 membrane translocation through the activation of AMPK pathway, in a PI-3-K/AKT-independent manner Increases insulin secretion increased plasma and colonic active GLP-1 (7-36) amide secretion	67 68-69
15	*Pterocarpusmarsupium*Roxb(Fabaceae) Heartwood, bark	Enhances insulin secretion Conversion of proinsulin to insulin & cathepsin B activity	71-73
16	*Scoparia dulcis* L. (Scrophulariaceae) Whole Plant	PPAR-γ agonistic activity Increases insulin secretion	74 76

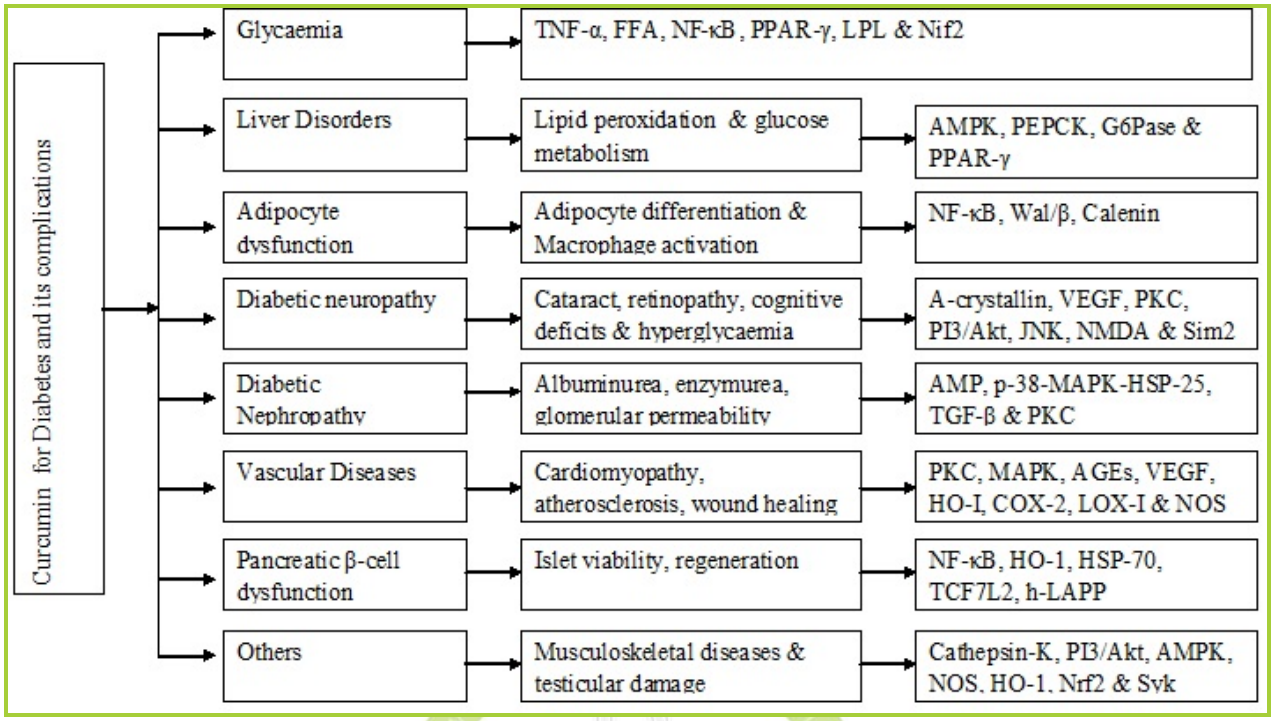
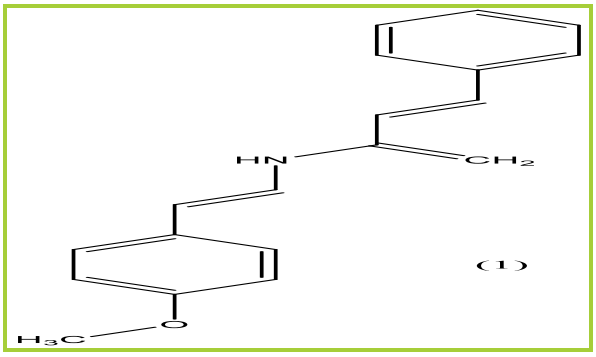


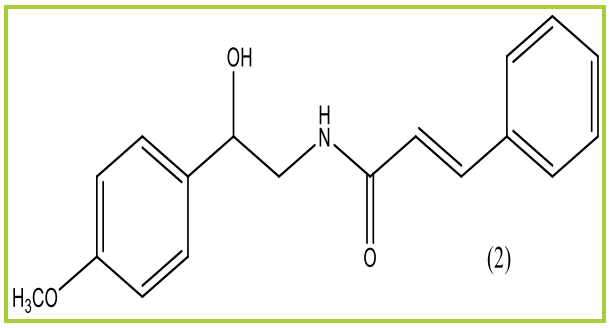
Fig: 1 The relevant molecular targets of diabetes and it complications modulated by curcumin

Bael leaves normalizes the hyperglycemia-induced endothelial dysfunction and activation, attenuate the early stages of diabetic cardiomyopathy and nephropathy.[9-10] The combination of A. marmelos and pyridoxine reported exhibiting neurodegeneration affecting the motor ability of an individual by serotonergic receptors (5-HT 2A), which has clinical significance in the management of diabetic neuropathy.11 The bael leaf showed to delay the cataract formation by protecting the antioxidants, which contribute to the integrity of α-crystallin's chaperone activity and inhibiting the lens aldose-reductase.[12]

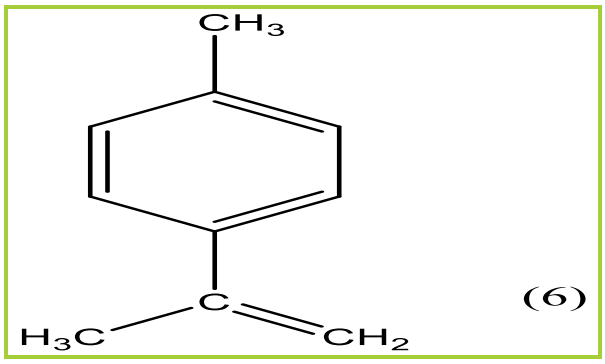
The phytochemicals - **anhydroaegeline (1), aegeline-2 (2), umbelliferone α-D-glucopyranoside (UFD) (3), umbelliferone β-D-galactopyranoside (UFG) (4),** reported as potent α-glucosidase inhibitors. They reduce postprandial hyperglycemia by enhancing the release of insulin and antioxidant enzymes.[13-14] **Umbelliferone (5)** shown a beneficial effect even in collagen-mediated polyneuropathy, nephropathy and normalizes prothrombin, clotting and bleeding time in diabetic rats.[15] **Limonene (6), scopoletin (7)** shown nephroprotective, delay the cataract formation in diabetic rats.[16-17] Bael fruits improve the insulin resistance and β-cell regeneration in rats through increased peroxisome proliferator-activated receptor-γ (PPARγ) expression.[18] Fifteen days clinical trial, the bael leaf has reported significant hypolipidaemic and lowered the blood glucose.



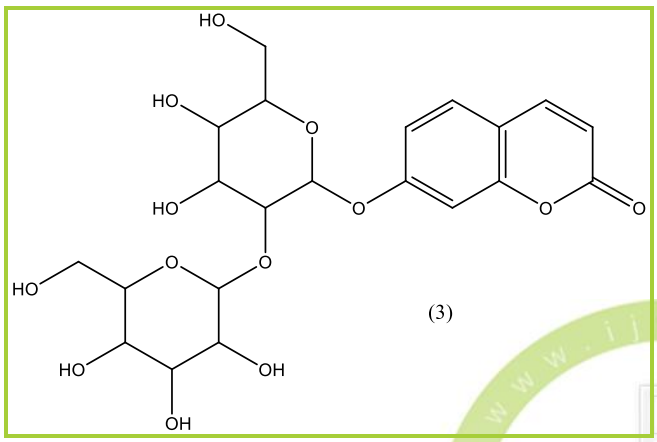
Anhydroaegeline (1)



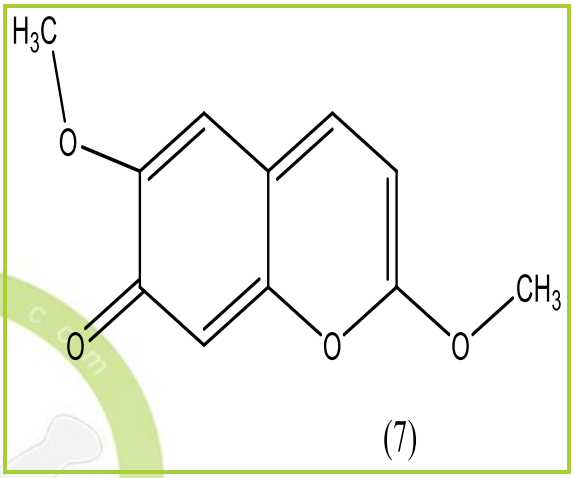
Aegeline-2 (2)



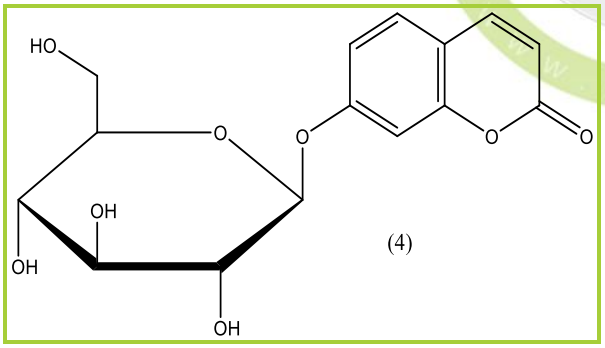
Limonene (6)



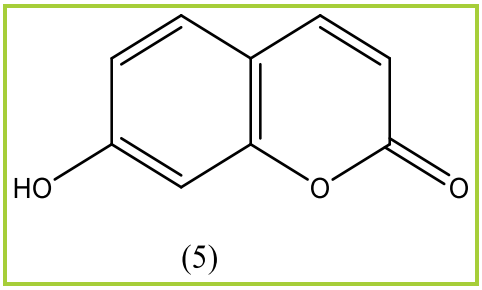
Umbelliferone α-D-Glucopyranoside (UFD) (3)



Scopoletin (7)



Umbelliferone β-D-Galactopyranoside (UFG) (4)

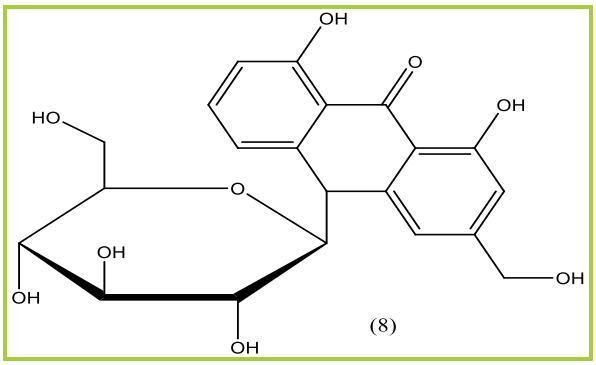


Umbelliferone (5)

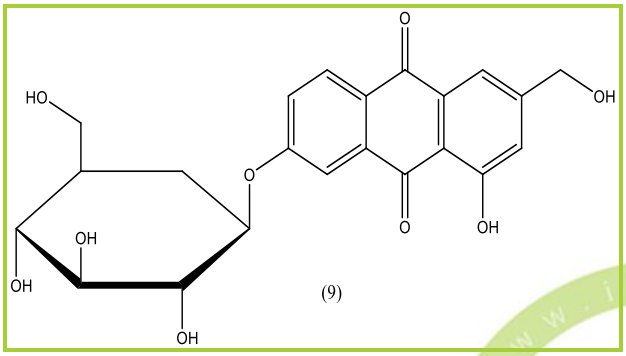
2. *Aloe vera* (L.) Burm. F (Alliaceae)

The phytosterols of *A. vera*, **lophenol (11)**, 24-methyl-lophenol, 24-ethyl-lophenol, **cycloartenol (12)** and 24-methy-lene cycloartenol shown antidiabetic effects by enhancing the insulin release.[19] **Aloin (8)**, aloe **emodin-8-O-glycoside (AEG) (9)** and aloe-**emodin (10)** were potent α-glucosidase inhibitors, antihyperglycemic activity by inhibiting the glycogen synthase kinase-3β in L6 myotubes and 3T3L1 adipocytes.[20-21]

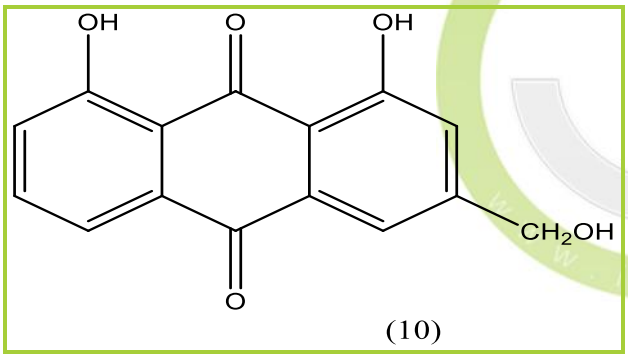
Additionally, *Aloe vera* gel has shown hypolipidemic and cardioprotective, antioxidant properties.[20-21] They act by upregulation of GLUT-4 mRNA synthesis, enhance the hepatic β-oxidation enzymes (ACO, CPT1) and PPARα expressions in liver.[22-23]



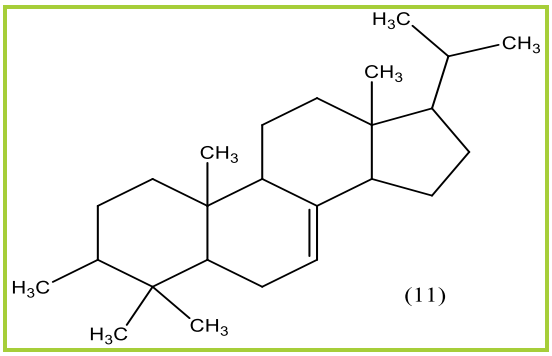
Aloin (8)



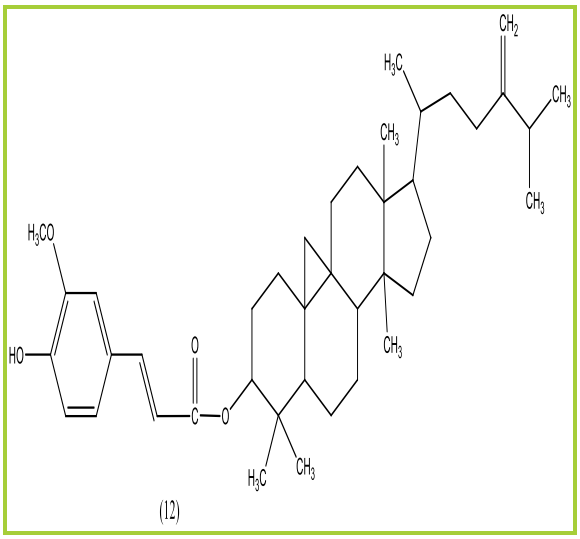
Emodin-8-O-Glycoside (AEG) (9)



Emodin (10)



lophenol (11)



Cycloartenol (12)

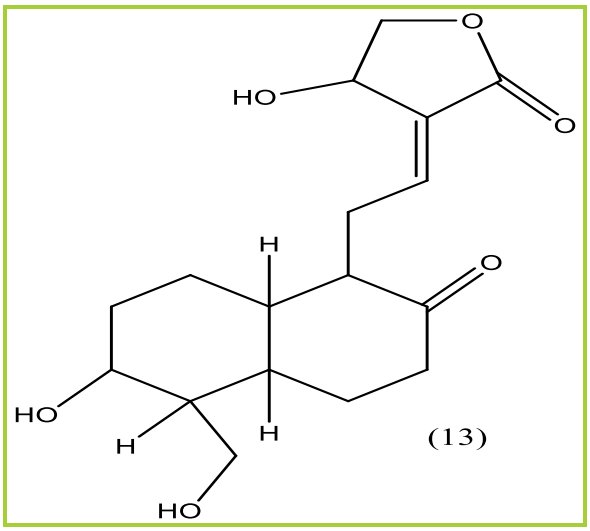
Pre-clinical and clinical studies reported the gum and sap of *aloe vera* enhance the glucose tolerance in both normal and diabetes. The *aloe vera* gel compound reduced body weight, BFM, and insulin resistance in clinical studies.[24] *Aloe Vera* gel shown to lower the fasting blood glucose, HbA1c, total cholesterol, and LDL levels significantly in a double-blind placebo-controlled clinical trial with hyperlipidaemia T2DM patients.[25] The *aloe vera* juice in combination with glibenclamide significantly reduced fasting blood glucose within two weeks and triglycerides within four weeks in diabetic patients.[26] The oral administration of one table spoonful of *aloe vera* juice, twice a day for 2 weeks well managed the serum glucose and triglycerides in diabetic patients.[27]

3. *Andrographis paniculata* (Burm. f.) Wall. (Acanthaceae)

The andrographolide, isolated from *A. paniculata* shown significantly reduced blood glucose by stimulating GLUT4 translocation, improve beta cell functions at 50 mg/kg. The

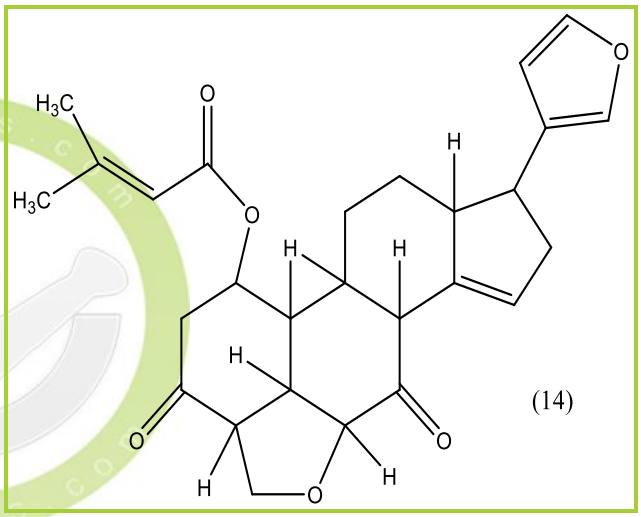
oral administration of ethanol extracts reported significantly reduced the fasting blood glucose clinically. Some other bioactive compounds namely 14-deoxy-11,12-didehydroandrographolide also reported the antihyperglycemic activity.

Andrographolide (13) reported preventing the onset of insulitis in a dose dependent manner. It may act by regulating the Th1/Th2/Th17 homeostasis through which it prevents *β*-cell death and inhibit T-cell infiltration into pancreatic islets and thereby avoid the development of T1DM. Recent studies revealed that *A. paniculata* enhances glucose utilization, restore insulin signaling molecules in the liver.



Andrographolide (13)

Additionally, aqueous extract and active constituents (andrographolide and neoandrographolide) of *A. paniculata* exhibited significant antihypertensive activity, platelet anti-aggregation *in vitro* and *ex vivo* assays.[28]Recent article revealed the 15-p-chlorobenzylidene-14-deoxy-11, 12-didehydro-3, 19-dinicotinateandrographolide was found potent alpha-glucosidase inhibitor.[29]

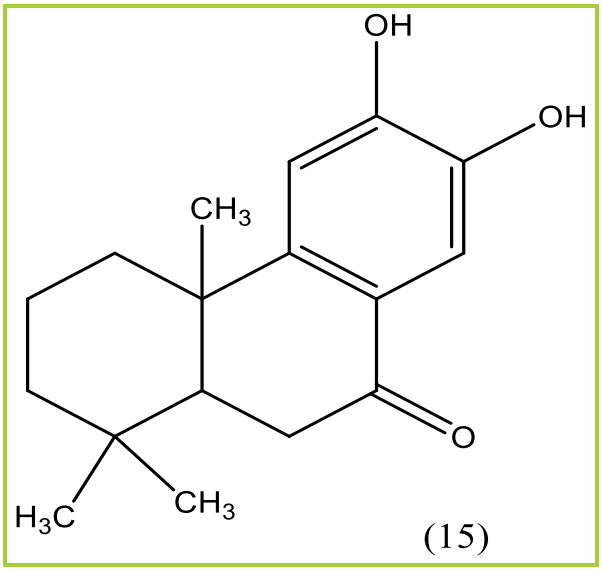


Meliacinolin (14)

4. *Azadirachta indica* A. Juss (Meliaceae)

The fresh leaves of neem and fruit were reported significant antidiabetic effect in preclinical studies. Additionally, the plant completely reversed the unusual changes in the retina in diabetic rats.[30]

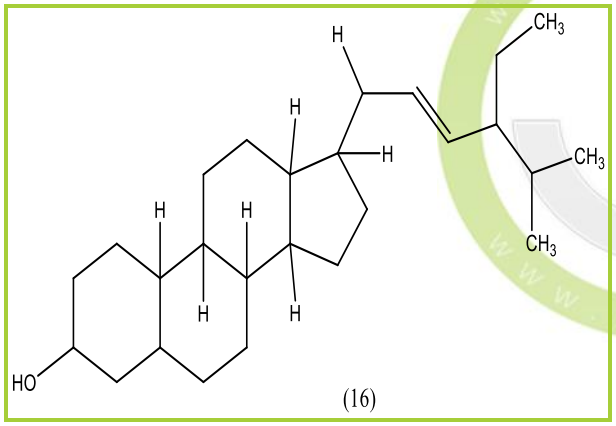
The bioactive compounds - **Meliacinolin (14), Nimbidiol (15)** reported to have α-glucosidase and α-amylase inhibitory activity and efficiently reduces insulin resistance, oxidative stress and improves the renal function, lipid abnormalities in diabetic mice.[31-32] It also reported significantly reduces the AGE formation. Clinical reports revealed the seed juice has significant control over the blood glucose in uncontrolled diabetic patients.[33]



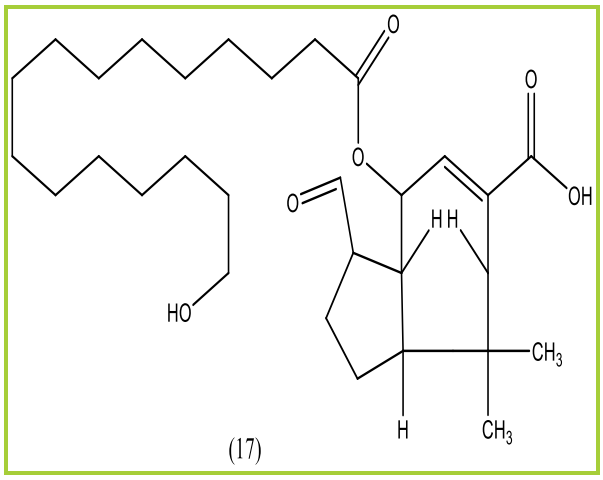
Nimbidiol (15)

5. *Butea monosperma* Lam. (Fabaceae)

The single dose and multiple doses of ethanolic extract of *B. monosperma* bark reported improving the glucose tolerance and antidiabetic effect in laboratory animals. They may act by enhancing the insulin secretion and increased glycogen formation in the liver.[34-35] **Stigmasterol (16)**, isolated from the bark of *B. monosperma* revealed to reduce the serum triiodothyronine, thyroxine and glucose concentrations. It may show antidiabetic activity by reduced activity of hepatic glucose-6-phosphatase (G-6-Pase).[36] **Laccijalaric ester-I (17)**, a triterpene present in soft resin of *B. monosperma* seeds shown significant hypoglycemic, antioxidant activity by enhancing hepatic glycogen and exerts a protective effect on the declined activity of SOD, CAT, GSH-Px in different tissues.[37-38]



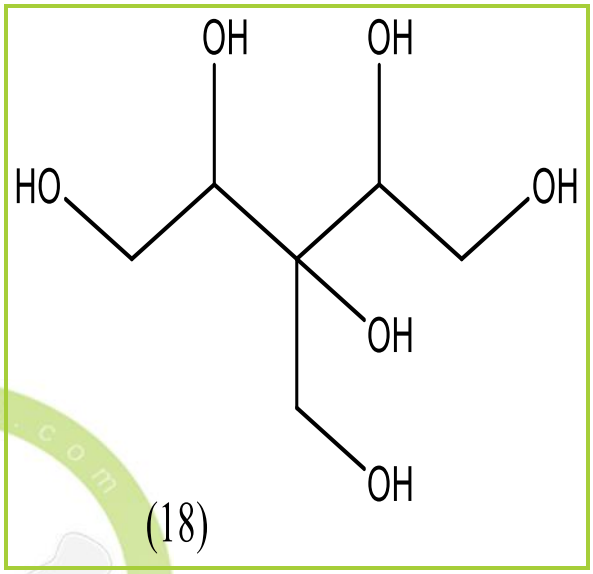
Stigmasterol (16)



Laccijalaric ester-I (17)

6. *Casearia esculenta* Roxb.(Samydaceae)

The root of *C. esculenta* reported possessing antihyperglycemic, antioxidant, hypolipidemic activity in diabetic rats. The presence of **3-(Hydroxymethyl) xylitol (18)** in root is responsible for the activity.[39-43]



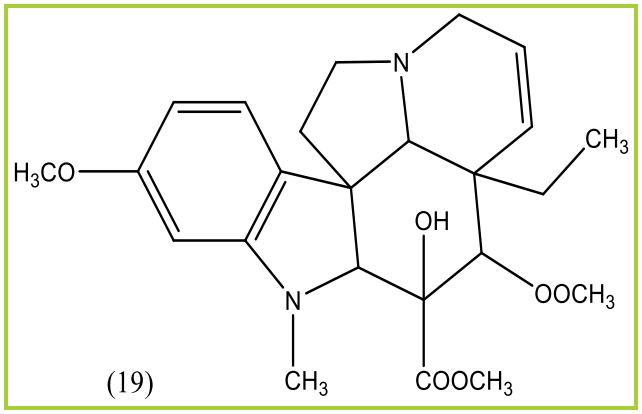
3-(Hydroxymethyl) xylitol (18)

7. *Catharanthus roseus* L. (Apocyanaceae)

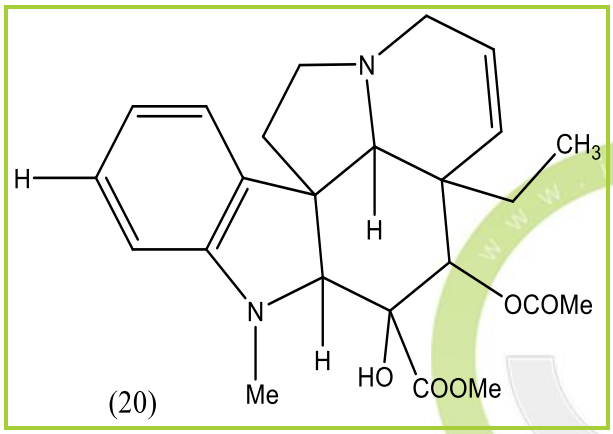
The leaves and flowers of *C. roseus* reported antidiabetic activity in dose dependently. Vindoline, an alkaloid of *C. roseus* reported enhancing the insulin secretion, protecting the pancreatic β-cells from the cytokine-induced apoptosis in insulinoma MIN6 cells and primary pancreatic islets. This effect may be due to Kv2.1 inhibition, which reduces the voltage-dependent outward potassium currents and finally enhancing insulin secretion.[44]

The four alkaloids- **vindoline I (19), vindolidine II (20), vindolicine III (21) and vindolinine IV (22)**- were also isolated leaves. They revealed relatively high glucose uptake in pancreatic β-TC6 or myoblast C2C12 cells and III has the highest activity. Compounds II-IV indicated to have good protein tyrosine phosphatase-1B (PTP-1B) inhibitory activity,

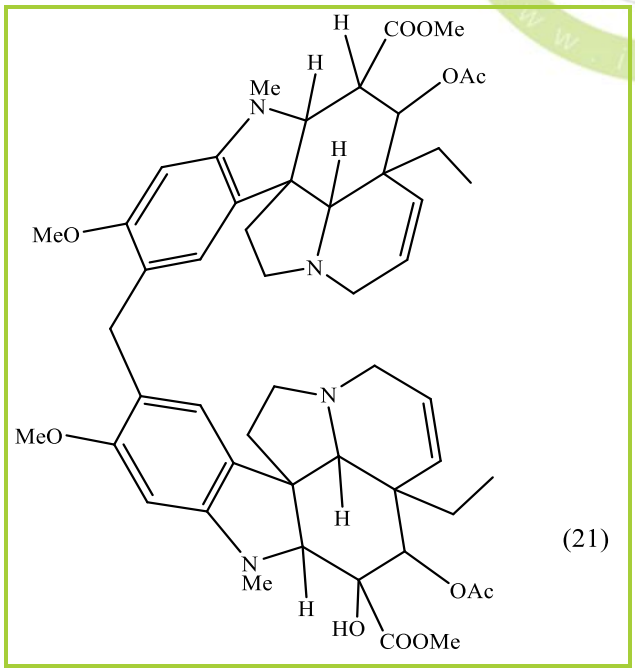
implying their therapeutic potential against T2DM.[45]



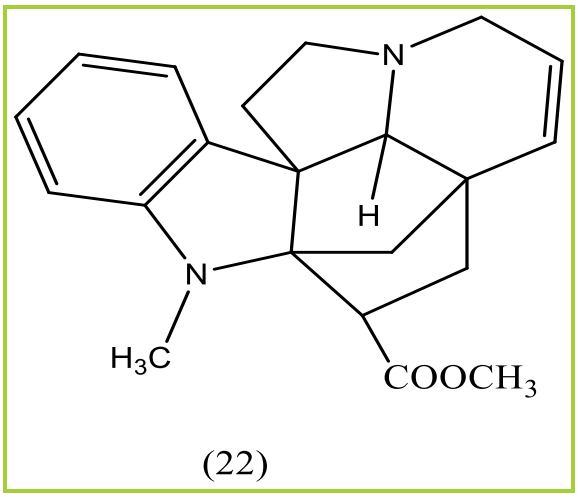
vindoline I (19)



Vindolidine II (20)



Vindolicine III (21)



Vindolinine IV (22)

8. *Cinnamomum zeylanicum* Blume(Lauraceae)

Cinnamaldehyde, isolated from the *C. zeylanicum* demonstrated a significant reduction of plasma glucose and HbA1c levels in stz-induced diabetic rats by increasing insulin secretion. Water-soluble polyphenol polymers such as trimers and tetramers of the flavonoids, catechin, and epicatechin were isolated from cinnamon reported to increase the insulin-dependent in vitro glucose metabolism roughly 20-fold and display antioxidant activity. These cinnamon polyphenols (CP) with doubly linked procyanidin type-A polymers appear to be unique for their insulin-like activity. The other compounds of cinnamon that showed little or no insulin like activity are cinnamic acid, cyanamide, cinnamyl alcohol, eugenol and 2-methoxy cinnamaldehyde under the assay conditions of the study.

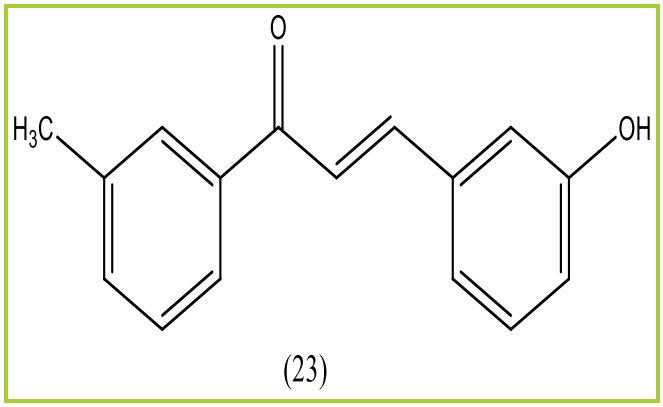
The cinnamon exerted its antidiabetic activity at different levels of the insulin-signaling pathway as given below. Cinnamtannin B1, a proanthocyanidin isolated from the stem bark of *Ceylon cinnamon*, activates the phosphorylation of the insulin receptor β-subunit on adipocytes as well as other insulin receptors. Cinnamaldehyde treatment in C_2C_{12} skeletal muscle cells resulted in a significant increase in the expression of GLUT 4 receptor and its mRNA. Cinnamldehyde increases the GLUT 1

mediated glucose uptake in a dose dependent manner in the L 929 fibroblasts. Cinnamon extract ameliorates type-2 diabetes by inducing GLUT4 translocation via the AMPK signaling pathway, increases GLUT4 receptors, Insulin Receptor (IR) and IR substrates and thereby facilitating glucose entry into cells. The extracts of *C. zeylanicum* reported increasing the production and translocation to the plasma membrane of the GLUT 4 in brown adipose tissue and muscle in a dose dependent manner from 42.8 % to 73.1 % in cinnamon treated rats.

Cinnamon treatment resulted in dose dependent reduction of serum insulin concentrations and an increase in glucagon like peptide-1 (GLP-1). An addition of 3 g of cinnamon to a rice meal caused a significant increase of GLP-1 levels with decreased serum insulin. Improved glucose transport across the cell membrane reduces the insulin resistance, and this probably accounts for the reduced insulin levels. Cinnamon causes an increase in the expression of PPAR (α) and PPAR (γ), thereby increasing insulin sensitivity in in-vitro and in vivo in mouse adipose tissue. Cinnamon showed the inhibitory effects on intestinal maltase and sucrase, pancreatic α-amylase, and their combined effect in the presence with acarbose. Cinnamon treatment demonstrated the stimulation of glycogen synthesis and inhibition of gluconeogenesis, improving glucose metabolism. An addition of cinnamon with 6g delayed in rice pudding delayed the gastric emptying but caused a more pronounced reduction in post prandial blood glucose and did not affect satiety in 14 healthy adults.

Till date, several randomized controlled studies exist that examined the effect of cinnamon on type 2 adult diabetic patients. These studies variable reviewed the effect of cinnamon on glycosylated hemoglobin, FPG, total cholesterol, LDL cholesterol, and triglycerides. The randomized, double blind clinical study demonstrated that an addition of 3 g of cinnamon aqueous extract per day for four months significantly decreased 10.3% of the initial FPG values. This indicated that patients with a higher initial glucose might benefit more from the addition of cinnamon. In another clinical study, the administration of 1 g of cinnamon capsules daily for 90 days to type 2 diabetic patients indicated a significant reduction of their HbA1c by 0.83 % as opposed to 0.37 % reduction in patients receiving usual care alone. Roussel et al. investigated the effect of dried aqueous extract of cinnamon at dose 500 mg/d for 12 weeks significantly reduced the fasting glucose and improvement in plasma oxidative stress markers. Shen et al. studied the effect of cinnamon at variable doses on the glycemic effect and renal functions of STZ-induced diabetic rats. Animals receiving cinnamon extract in doses exceeding 30 mg/Kg, demonstrated a reduction in creatinine values. This high coumarin content of *C. cassia* and other species has led some agencies to advocate against the regular use of *C. cinnamon* as a supplement in diabetes. On the other hand, the very low content of coumarins found in *cinnamomumzeylanicum*makes it a potentially useful medication or supplement for long-term use.[46-47]

Cinnamaldehyde (23), cinnamon polyphenols, cinnamon oil, are the principal components, which exhibit antidiabetic, antihyperlipidemic activity in diabetic rats. They act by various mechanisms such as repairing pancreatic beta cells, improving its anti-oxidative capacity, attenuating cytotoxicity via inhibition of iNOS, NF-κB activation, upregulation of mitochondrial UCP-1, and enhanced translocation of GLUT4 in the muscle and adipose tissues, improvement in muscle and hepatic glycogen content.[48-49]



Cinnamaldehyde (23)

9. *Curcuma longa* L. (Zingiberaceae)

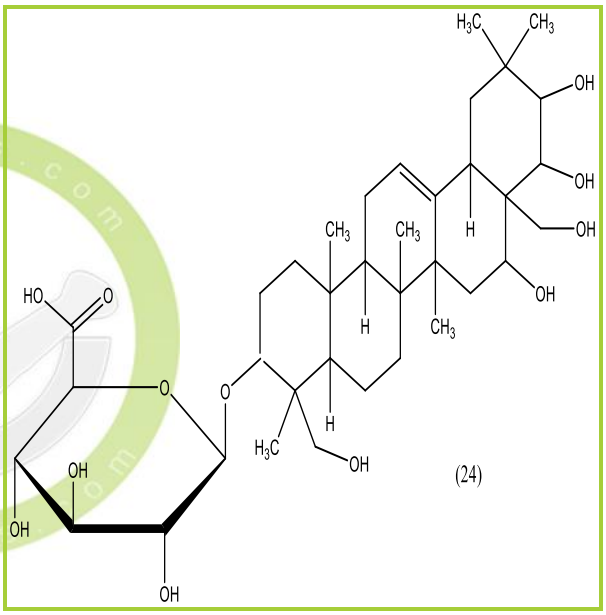
The literature on curcumin reported having hypoglycemic, diabetes-related liver disorders, adipocyte dysfunction, neuropathy, nephropathy, vascular diseases, pancreatic disorders and also antioxidant and anti-inflammatory properties. *Curcuma longa* reported containing novel anti-diabetic molecules such as curcumin and curcuminoids as demethoxycurcumin (DMC), Bisdemethoxycurcumin, Tetrahydrocurcumin (THC), Bis-1, 7-(2-hydroxyphenyl)-hepta-1,6-diene-3,5-Dione, Bis-o-hydroxycinnamoyl methane, Bis(curcumino)oxovanadium complex. Curcumin is actively involved in treating DM and its complications which such as liver disorders, adipocyte dysfunction, neuropathy, nephropathy, vascular diseases, pancreatic β-cell dysfunction, and other complications.[50-51] The curcumin has the various molecular targets and modulates the cofactors involved in the pathophysiology of DM and its complications shown in figure 1, and some of them made as drug targets for other drugs also.

10. *Ficus racemosa* Linn (Moraceae)

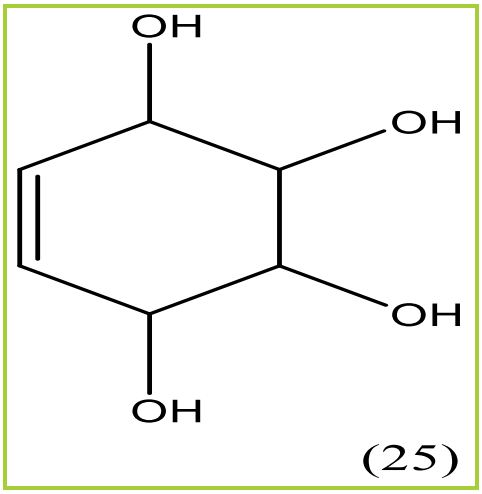
The stem bark, fruits leaves of *F. racemosa* reported significant hypoglycemic activity in alloxan-induced diabetic rats. The β-sitosterol, isolated from the stem bark is responsible for the hypoglycemic activity . The hypoglycemic effect of this plant may be due to α-glucosidase& α-amylase inhibitory activity.[52-54]Bio-activity guided isolation reported the potent antidiabetic chemical- alpha-amyrin acetate, which lowers blood glucose levels by 18.4 and 17.0% at 5 and 24 h, respectively, in sucrose, challenged stz-induced diabetic rats (STZ-S).[55]

11. *Gymnema Sylvestre* R. Br. (Asclepiadaceae)

Previous studies have demonstrated that Gymnema may exert its antidiabetic effect via a number of pathways and some are similar to those produced by existing oral hypoglycemic agents. A leaf of *G. sylvestre* leaves reported regeneration of pancreatic tissue by 30% increase in total pancreatic weight, as well as a significant increase in the number of islets ($p<0.001$) and cells per islet ($p<0.05$). The phytoconstituents -**deacylgymnemic acid (24) and conduritol A (25)** were responsible for the hypoglycemic, hypolipidemic activity and enhanced β-cell numbers of pancreas in rats.[56-59]The leaf of *G. sylvestre* at 400 mg b.i.d. for 90 days demonstrated that decrease in preprandial blood glucose level (BGL), postprandial BGL and HbA1c by 11%, 13%, and 0.6% respectively in clinical studies. It also significantly increased serum C-peptide levels at 16–18 months in T1DM patients.[60]



Deacylgymnemic acid (24)



Conduritol A (25)

12. *Melia azedarach* Linn. (Meliaceae)

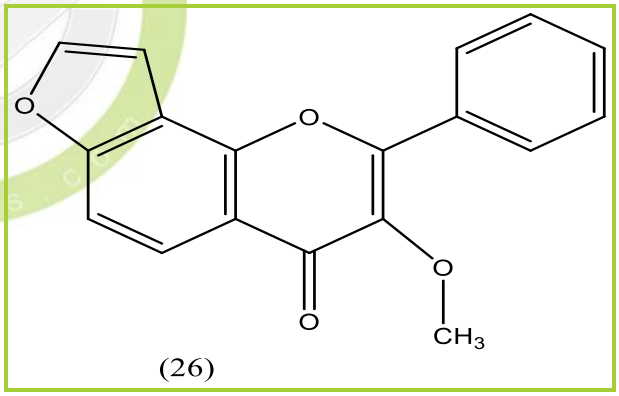
The ethanolic extract of the leaves of *M.azedarach*at 600 mg/kg and 300 mg/kg for twenty-one days in glucose loaded rats showed significant antidiabetic activity.[61] The n-hexane, chloroform, ethyl acetate, n-butanol and aqueous fractions of the methanolic extract of fruits of *meliaazedarach* at a dose of 50 mg/kg in healthy rabbits for 40 days demonstrated that all the extracts possess hypoglycemic, hypolipidemic and HDL boosting properties. The only aqueous fraction was found safe. The chloroform and butanol fractions isolated from *M. azedarach* fruits and leaves through bioassay guided procedure exhibited significant PTP-1B inhibition activity together with glucose uptake stimulation in cell cultured C2Cl12 myoblasts. The isolated pure compounds may be euphane type of triterpenoids, could be further explored to develop therapeutic or preventive agents for the effective complementary treatment for T2DM.[61-64]

13. *Ocimum sanctum* Linn. (Lamiaceae)

The ethyl acetate, petroleum ether and chloroform fractions of ethanolic extract of the leaves of *Ocimum sanctum* at 200 mg/kg, IP, reported to reduce FBG level by 80.19%, serum TC and TG level of 54.49 and 79. 78% respectively and elevation of liver glycogen in alloxan induced diabetic rats. It also reported having significant hepatoprotective property. It also decreases the serum cortisol and glucose and exhibited the antiperoxidative effect.[65]The tetracyclic triterpenoid isolated from hydro alcoholic extract of aerial part of *O. sanctum* by column chromatography was found to be potent anti-diabetic effect in alloxan induced rats.[66]

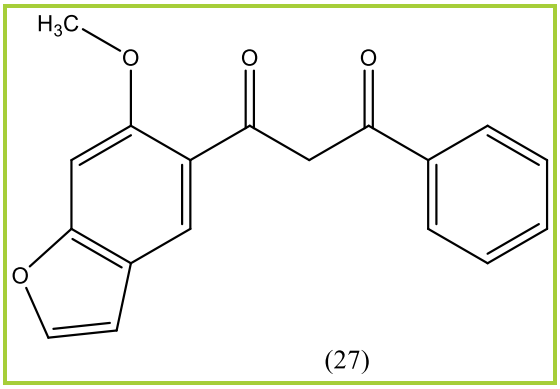
14. *Pongamia pinnata* (Linn.) Pierre (Leguminosae)

A lead molecule **karanjin (26)**, isolated from the fruits of *P. pinata* exhibited a substantial increase in the glucose uptake in L6 myotubes. This results from an increased translocation of GLUT4 to plasma membrane associated with activation of AMPK pathway, in a PI-3-K/AKT-independent manner. Another molecule, **pongamol (27)** isolated from the fruits of *P.pinnata*, promoted the glucose transport and GLUT4 translocation to the plasma membrane, driven by a PI-3-K/AKT dependent mechanism in L6 myotubes. The pongamol and karanjin possesses significant antihyperglycemic activity in Streptozotocin-induced diabetic rats and type 2 diabetic db/db mice, and protein tyrosine phosphatase-1B may be the possible target for their activity.[67] **Cycloart-23-ene-3beta, 25-diol (28)** isolated from the stem bark of *P. pinnata* at (1mg/kg and 3mg/kg) significantly reduced HbA1c may act by increased pancreatic insulin secretion and antioxidant activity in STZ-nicotinamide induced diabetic mice. The docking study suggested that cycloart-23-ene-3β, 25-diol bound to the GLP-1 receptor and decreases the plasma glucose level, increased plasma and pancreatic insulin level as well as increased plasma and colonic active GLP-1 secretion in STZ-nicotinamide induced diabetic Sprague-Dawley's rats.[68-69]



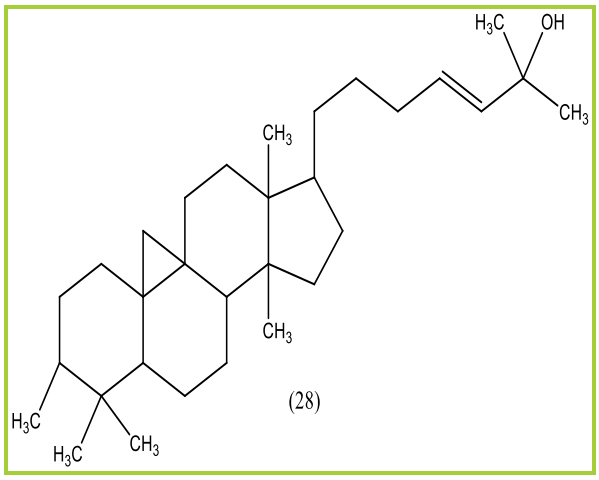
(26)

karanjin (26)



(27)

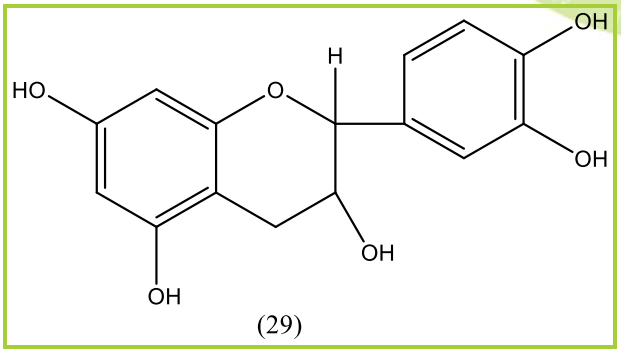
Pongamol (27)



Cycloart-23-ene-3beta, 25-diol (28)

15. *Pterocarpus marsupium* Roxb (Fabaceae)

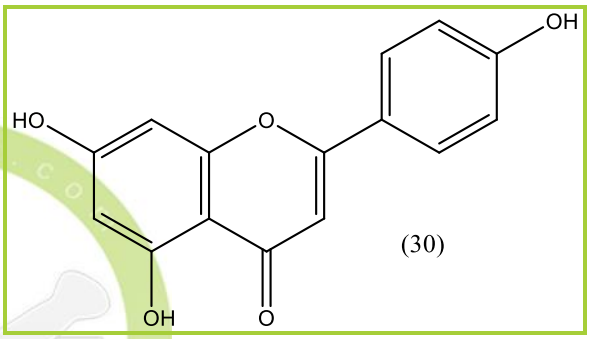
The phenolic components, marsupsin, and pterostilbene were isolated from the heart wood of *P. marsupium* significantly lowered the blood glucose in hyperglycemic rats.[70] An active constituent **(-)-epicatechin (29)**, isolated from the bark of the *P. marsupium* reported having insulin like properties. It stimulates glucose uptake in fat cells, and tissue slices of various organs increase glycogen content of rat diaphragm in a dose-dependent manner. It also reported increasing insulin release, conversion of proinsulin to insulin and cathepsin B activity.[71-73]



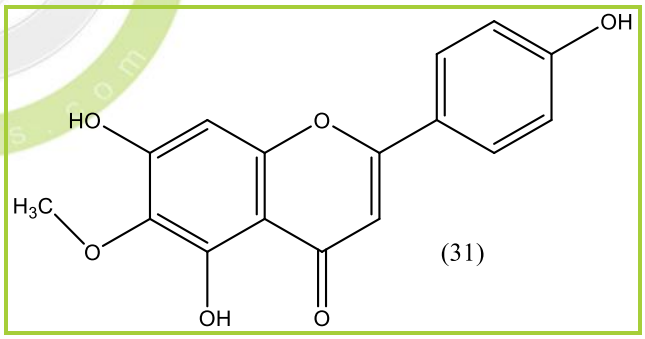
(-)-Epicatechin (29)

16. *Scoparia dulcis* L. (Plantaginaceae)

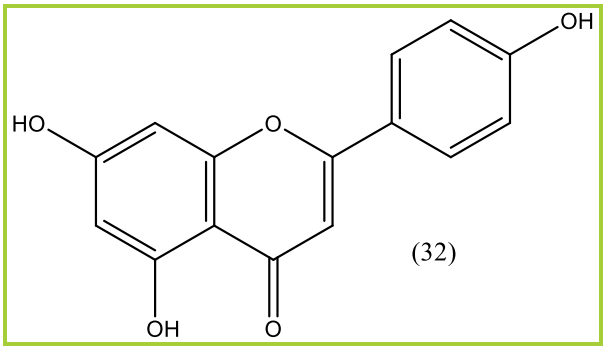
Diterpenoids, 4-epi-7α-O-acetyl-scoparic acid A, and flavonoids- **scutellarein (30), hispidulin (31), apigenin (32), and luteolin (33) and acerosin (34)** were isolated from the *S. dulcis* plant exhibited peroxisome proliferator-activated receptor gamma (PPAR-γ) agonistic activity.[74] The TLC fraction-7 (SDF7) from the extract of *S.dulcis* reported glucose uptake properties as potent as insulin at a maximum concentration of 50 µg/ml at 480 min on L6 myotubes.[75] A diterpenoid, **scoparic acid D (SAD) (35)** isolated from the ethanolic extract of *S. dulcis*at a dose of 10, 20 and 40 mg/kg for 15 days exhibited a significant increase in plasma insulin levels. Further, the SAD was tested on STZ-treated rat insulinoma cell lines (RINm5F cells) and isolated islets in vitro, which showed at a dose of 20 µg mL(-1) evoked two-fold stimulation of insulin secretion from isolated islets, indicating its insulin secretagogue activity.[76]



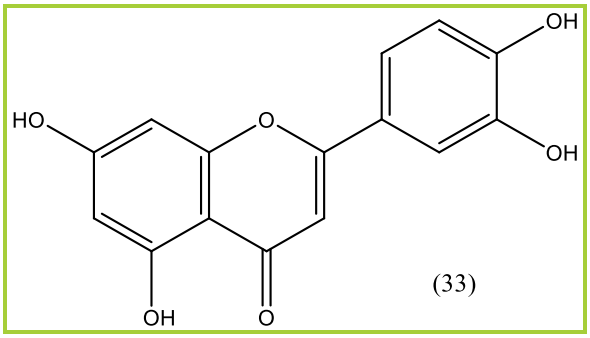
Scutellarein (30)



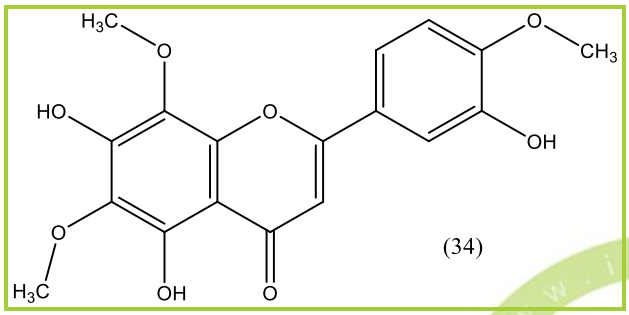
Hispidulin (31)



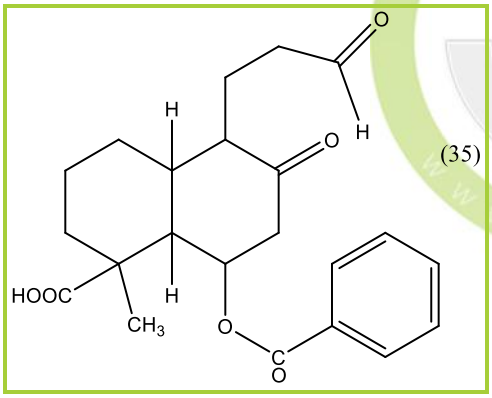
Apigenin (32)



luteolin (33)



Acerosin (34)



D (SAD) (35)

CONCLUSION

Diabetes is a metabolic disorder characterized by diminished production of insulin or insulin resistance. Based on the WHO recommendations, hypoglycemic agents of plant origin used in traditional medicine are important. Herbal treatments for diabetes have been used in patients with insulin-dependent and non-insulin-dependent DM, diabetic retinopathy, diabetic peripheral neuropathy, etc. From the scientific reports on their potential effectiveness against DM, it is assumed that the botanicals have a significant role to play in the management of DM, which needs further exploration for necessary development of drugs and nutraceuticals from natural resources. This review provided the various secondary metabolites of western that medicinal plants possessing beneficial effects in the management of DM and its associated complications. Above mentioned secondary metabolites and medicinal plants have not undergone careful scientific assessment and some have the potential to cause serious toxic effects and major drug-to-drug interaction. Continuing research is necessary to find novel molecules for the management of diabetes mellitus and its associated complications.

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