

Phytotherapies for diabetes

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Abstract

Plant medicines (phytotherapies) have a long history as treatments for diabetes. With a disturbing rise in the prevalence of this metabolic disease and associated healthcare costs, interest in alternative or complementary therapies has grown. Over the last 10-20 years, data from controlled investigations in animal models and patients have validated the therapeutic value of numerous phytotherapies for diabetes. Phytotherapies and their combinations demonstrate multiple beneficial antidiabetic mechanisms, including modulation of carbohydrate metabolism, restoration of β -cell integrity and function, insulin-releasing activity, improvements in glucose uptake/utilization, antioxidant properties and a reduction in the risk of cardiovascular disease. However, there is also a misconception that natural remedies are entirely safe. This article summarizes several of the most extensively studied phytotherapies for diabetes and its complications, indicating important associated adverse effects that should be considered when using natural therapies. More than 170 antidiabetic constituents isolated from over 170 plants are presented.

Introduction

Diabetes mellitus is a complex metabolic disorder characterized by a decrease in or cessation of insulin secretion in response to physiological stimuli, or reduced responsiveness of peripheral tissues to insulin. Type 1 diabetes, or insulin-dependent diabetes, is characterized by selective, immune-mediated destruction of over 90% of insulin-secreting pancreatic β -cells. This autoimmune response means that type 1 diabetic patients are dependent on insulin injections to control blood sugar. Type 2 diabetes, or non-insulin-dependent diabetes, causes hyperglycemia as a result of impaired insulin secretion in response to glucose and decreased insulin effectiveness (insulin resistance). Type 2 diabetes is far more common and accounts for 90-95% of all cases (1). However, the treatment of type 2 diabetes is complicated by several factors inherent to the disease process, such as insulin resistance, hyperinsulinemia, impaired insulin secretion and reduced insulin-mediated glucose uptake and utilization (2). While some cases of type 2 diabetes can be controlled by weight loss and diet alone, in some instances the use of insulin or oral hypoglycemic drugs, such as sulfonylureas and biguanidines, is necessary to help normalize blood glucose. If untreated, diabetes can lead to severe complications, including atherosclerosis, retinopathy and neuropathy, as well as ulceration and gangrene of the extremities. Recent figures from the Centers for Disease Control and Prevention (CDC) indicate that the prevalence of diabetes in the U.S. during 2005 was 20.8 million (7% of the population; 14.6 million diagnosed and 6.2 million undiagnosed), with total estimated costs for 2002 arriving at an alarming USD 132 billion (3). Diabetes shows no signs of abating, with an aging population, unhealthy diet, obesity and sedentary lifestyles (4), and the WHO predicts that by the year 2025 the prevalence of this metabolic syndrome will be nearly 300 million.

Before the advent of insulin, diabetes was treated with plant medicines (phytotherapies). More than 1,200 species have been reported for the treatment of this metabolic disorder (5), although only a relatively small proportion of them have been subjected to scientific and medical evaluation, predominantly in type 2 diabetes. With regard to patient appeal, recent U.S. national sur-

veys have reported that the frequency of use of complementary and alternative phytotherapies among diabetic patients varies from 33% for the general population to 49% for the Hispanic population in South Texas (6). In the last 10-20 years, several studies have presented data on numerous phytotherapies that appear to be effective as glucose-lowering agents, with no or very few associated adverse effects (7). Phytotherapies demonstrate multiple beneficial antidiabetic mechanisms, including modulation of carbohydrate metabolism, restoration of the integrity and function of β -cells, insulin-releasing activity, improvements in glucose uptake/utilization, antioxidant properties and a reduced risk of cardiovascular disease. The following is a summary of several of the most extensively studied and commonly used phytotherapies for diabetes.

***Allium* spp.**

Both *Allium cepa* (onion) and *Allium sativum* (garlic) have demonstrated glucose-lowering properties (8) that are thought to be due to the action of their sulfur-containing compounds allylpropyl disulfide (APDS) (9) and disulfide oxide (allicin) (10), respectively. However, flavonoids may also play an additional role in the observed effect (7). Experimental and clinical studies suggest that APDS lowers glucose levels by competing with insulin for insulin-inactivating sites in the liver, resulting in an increase in free insulin. Mechanisms of action include increased secretion or slowed degradation of insulin, increased glutathione peroxidase action and improved liver glycogen storage (11). Clinical evidence has also demonstrated the antioxidant properties and beneficial cardiovascular effects (*i.e.*, cholesterol- and blood pressure-lowering action) of these compounds (12).

Aloe vera

Aloe vera, a plant resembling the cactus, is widely used for the treatment of burns and wounds. However, aloe dried sap and aloe gel are also well-known remedies for diabetes in the Arabian Peninsula. Aloe gel (obtained from the inner portion of the leaves) contains glucomannan, a hydrosoluble fiber that may help to reduce sugar (13) and triglyceride levels (14).

Ginseng

Ginseng root, possibly the most widely reported among the phytotherapies, has been used for over 2,000 years (15). *Panax ginseng* (Asian ginseng) and *Panax quinquefolius* (American ginseng) are the most popular species, although chemical composition and potency may vary depending on the age of the root, the location grown, the season of harvesting and the method of drying. The principal components responsible for the hypoglycemic activity are the triterpenoid saponin glycosides, commonly referred to as ginsenosides or panaxosides. They reportedly act by modulating portal hepatic circulation by

increasing glucose transport and uptake mediated by nitric oxide, and increasing glycogen storage and modulation of insulin secretion (11). Ginseng is reported to reduce the dose of insulin needed by patients, prolong the action of a dose of insulin and improve psychophysiological performance and physical activity, elevating mood and reducing body weight (16).

***Gymnema sylvestre* (Gurmar)**

This woody climber, which is native to the tropical forests of India, is commonly used in East Indian healing systems (Ayurveda) as a treatment for diabetes. It has also appeared on the U.S. market as a "sugar blocker". *Gymnema* extract has been shown to positively control both type 1 and 2 diabetes (7). It has been postulated that its active constituent, gymnemic acid, enhances the production of endogenous insulin, and both animal and human studies (17, 18) appear to support the possibility of pancreatic regeneration (7, 19).

Momordica charantia

Momordica charantia, also known as bitter melon, balsam pear or karela, is a tropical fruit grown in Asia, Africa and South America. It is the most popular plant used worldwide for diabetes (20). Daily dietary karela supplements have been shown to improve glucose tolerance (21), and several of its active constituents, such as charantin, vicine and polypeptide-P, demonstrate antidiabetic properties. Charantin, which is composed of mixed steroids, has been reported to have stronger hypoglycemic properties than the orally administered hypoglycemic agent tolbutamide (22). Insulin-like polypeptide-P, or plant insulin, with a similar effect to bovine insulin, has been shown to decrease blood sugar levels after subcutaneous injections in type 1 diabetic patients (15). The proposed mechanisms of action include increased insulin secretion, tissue glucose uptake, liver glycogen synthesis and glucose oxidation, and decreased hepatic gluconeogenesis (11).

Cinnamon

Cinnamon is a spice derived from the dried bark of a tropical evergreen tree. *In vitro* studies have indicated cinnamon-mediated improvement in insulin secretion (23, 24). A clinical study in type 2 diabetic patients also revealed that after 40 days of daily cinnamon supplements, mean fasting serum glucose, triglyceride, LDL cholesterol and total cholesterol levels were significantly reduced (25).

***Opuntia* spp.**

Opuntia spp. is known as nopal in Mexico or prickly pear cactus in the United States and produces both a vegetable called nopal and a fruit called tuna (20). Nopal is a common food source in Mexico. The proposed

mechanism of hypoglycemic action is partly due to the plant's highly soluble fiber and pectin content, which may affect intestinal glucose uptake. Furthermore, in addition to its positive effects on glucose control, both animal and human studies have demonstrated a significant *Opuntia*-associated reduction in total cholesterol levels (26-29).

***Trigonella foenum-graecum* (fenugreek)**

Fenugreek, a widely grown legume, is a common condiment in Indian cooking. It has been used as an appetite stimulant and to treat diabetes, migraines, allergies, elevated cholesterol and constipation (15, 20). The active constituents in fenugreek seeds are the alkaloid trigonelline, which has a hypoglycemic effect, and the amino acid 4-hydroxyisoleucine (ID-1101), which increases glucose-induced insulin release (20). In addition, fenugreek seeds contain over 50% fiber, which may indicate another potential mechanism for its beneficial effects in diabetes, as described below. Significant reductions in total cholesterol and triglycerides have also been documented with the use of fenugreek (30, 31).

Pterocarpus marsupium

Commonly used in India for the treatment of diabetes, *Pterocarpus marsupium* contains epicatechin (extracted from the bark of the plant), which has been shown to prevent pancreatic β -cell damage (7, 15, 32). In addition, both epicatechin and the crude alcohol extract from the plant have been shown to regenerate functional β -cells in diabetic animals (33). The different forms of catechin and epicatechin constitute a group of flavanones that are very strong antioxidants, particularly against hydroxyl radical-induced lipoperoxidation, characteristic of diabetes induced by alloxan and many hepatotoxins.

Silybum marianum

Silybum marianum, also known as milk thistle, is a member of the aster family. It has been studied primarily for its effect in alcoholic and viral hepatitis (11). Silymarin, an extract from the fruit of *S. marianum*, is rich in flavonoids, which are potent antioxidants, and has been shown to induce recovery of pancreatic function after alloxan-induced pancreatic damage in rats (34). Therefore, *S. marianum* might have a beneficial effect in patients with insulin resistance secondary to hepatic damage.

***Vaccinium myrtillus* (bilberry)**

The leaves of bilberry, a shrubby plant grown in Europe, have been widely used as treatments for diabetes. The anthocyanoside myrtillin is probably the most active constituent (15). Extracts from the berries provide a long-term hypoglycemic effect (35). Furthermore, anthocyanosides derived from this plant have affinity for

blood vessels of the eye and retina and show beneficial effects in diabetic retinopathy, macular degeneration, cataracts, retinitis pigmentosa and nightblindness (7, 36).

Catharanthus roseus

Also known as Madagascar periwinkle, or *Vinca rosea*, this plant, originally native to the island of Madagascar, has been used as a folk remedy for diabetes in Europe for centuries. *C. roseus* contains an abundant source of useful alkaloids, some of which, including catharanthine, leurosine sulfate, lochnerine, tetrahydroalstonine, vindoline and vindolinine, lower blood sugar levels, thus relieving the symptoms of diabetes. Evaluation of these antidiabetic effects has been carried out in animal models of the metabolic syndrome using leaf juice and an aqueous extract (37-39). All studies indicated the added advantage of control over lipid levels and enhanced antioxidant potential (39).

Galega officinalis

This plant, also known as goat's rue or French lilac, has been known for centuries to have natural benefits for diabetics, but its toxicity has prevented medicinal use (40). Guanidine, a chemical that is very similar to the active ingredient in goat's rue, galegin, was the inspiration for many conventional diabetic drugs, such as metformin hydrochloride. Metformin acts at multiple sites to increase tissue sensitivity to insulin (41) and targets the enzyme dipeptidyl-peptidase IV (DPP-IV), which cleaves and terminates the glucose-lowering effect of glucagon-like peptide-1 (GLP-1) (42). Metformin is now widely accepted as a safe oral treatment for type 2 diabetes, as monotherapy or in combination with insulin secretagogues and thiazolidinediones, and it can be of particular value for obese patients (for review, see 43).

Cyamopsis tetragonoloba

This vegetable, commonly consumed in southern India, is 20% guar gum, a soluble dietary fiber that has been suggested to be useful for the treatment of diabetes. High fiber intake can reduce and slow sugar absorption, and bulking agents are popular natural treatments for diabetes (44, 45). Both preclinical and clinical studies have demonstrated the hypoglycemic and hypolipidemic effects of guar gum (46-48). Furthermore, the cereal fiber *Hordeum disticum* (barley) and products containing high barley content have also been shown to reduce blood sugar and lipids and enhance insulin responses in animals and patients (49-52). The high chromium content of barley has also been postulated to play a role in the effects on these symptoms of diabetes (53). *Cichorium intybus* (chicory), a perennial plant, has also been shown to be beneficial for diabetic patients because of its high fiber content. Dietary insulin-type fructans extracted from chicory root promote the secretion of GLP-1 and its precursor proglucagon mRNA (54).

Multiple herb combinations and Chinese medicine

Chinese medical treatment of diabetes appears to date back to around 100 B.C. and includes herbal prescriptions, acupuncture and dietary recommendations. Combinations of herbs for the treatment of diabetes are widely used in traditional Chinese, Native American and Tibetan medicine (11, 15, 55). In modern China and Japan, there are now approximately 200 standard prescriptions reported to be suitable for treating diabetes. The majority of these may be viewed as combinations that rely primarily on about two dozen antidiabetic ingredients plus a small number of auxiliary herbs. The main traditional prescriptions include Rehmannia Eight Formula and its simplified version Rehmannia Six Formula, Ginseng and Gypsum Combination, and Ophiopogon and Trichosanthes Combination (56).

Other plants with hypoglycemic activity include *Acacia arabica*, *Artemisia herba-alba*, *Artocarpus heterophyllus*, *Atriplex halimu*, *Bauhinia forficata*, *Cleome drosifolia*, *Coccinia indica*, *Eugenia jambolana*, *Ficus bengalensis*, *Ficus carica*, *Ginkgo biloba*, *Glossostemon bruguieri*, *Lagerstroemia speciosa*, *Lythrum salicaria*, *Myrcia uniflora*, *Ocimum sanctum*, *Phaseolus vulgaris*, *Swertia chirayita*, *Swertia japonica*, *Tecoma stans*, *Teucrium polium* and *Vaccinium myrtillus* (11, 15, 57). In addition to the treatment of hyperglycemia, several natural products are used as complementary treatments for different diabetic complications. For example, evening primrose oil, extracted from the seeds of *Oenothera biennis*, as well as capsaicin, an ingredient in chilli pepper, have both received attention for their use in diabetic neuropathy (58-60). Potent inhibition of aldose reductase, the key enzyme of the polyol pathway, by tannoids of *Embolia officinalis* (amla) has been demonstrated to modulate the etiopathology of diabetic complications such as neuropathy, cataracts, nephropathy and retinopathy (61).

Adverse effects

Natural therapies are often misconceived to be entirely safe. However, ample evidence has been reported detailing the adverse effects of alternative remedies. For example, *M. charantia* can induce hypoglycemic coma and convulsions in children, reduced fertility in mice, a favism-like syndrome, increases in γ -glutamyltransferase and alkaline phosphatase levels in animals, and headache (62). Furthermore, *C. roseus* is better known for its cytotoxic anticancer alkaloids vinblastine and vincristine (63), and is therefore often associated with detrimental effects.

Alternative remedies can also negatively interact with conventional medicines (for reviews, see 64 and 65). Perhaps the most frequently reported example is that of ginseng, which has been shown to significantly and dan-

gerously decrease the anticoagulant effects of warfarin (66). The limited anticoagulant properties of garlic or trigonella can also be contraindicated when co-administered with warfarin (67, 68).

Nowadays, more and more patients are seeking alternative or complementary therapies to manage their diabetes. Although studies demonstrate that several of these natural remedies have potential for diabetes, there is insufficient evidence to actively recommend or discourage use. Product standardization and well-designed, rigorous clinical validation of safety, efficacy and the therapeutic risk/benefit ratio associated with the use of phytotherapies are essential. Several products derived from natural sources and targeted for diabetes are described in more detail below.

Caiapo (*Ipomoea batatas*) is a white sweet potato native to the Brazilian Amazon that is traditionally eaten raw as a treatment for anemia, high blood pressure and diabetes. In patients with type 2 diabetes, it has demonstrated long-term beneficial effects on plasma glucose, body weight, glycated hemoglobin and cholesterol levels (69, 70) by decreasing insulin resistance (69, 71). Caiapo is currently under phase II investigation at Fuji Sangyo and at the Universitaet Wien.

Preclinical studies have shown that LL-2113AD (GluDibit), an herbal adjuvant developed from dry extracts of five botanicals (*Gymnema sylvestre*, *Pterocarpus marsupium*, *Enicostemma littorale*, *Azadirachta indica* and *Salacia chinensis*), induces hypoglycemic effects in rats with streptozotocin-induced diabetes. A recent clinical trial evaluated the therapeutic benefits of add-on therapy with an oral formulation of LL-2113AD in adult patients with type 2 diabetes and uncontrolled hyperglycemia despite receiving oral hypoglycemic drugs for more than 6 months. After 4 weeks of LL-2113AD therapy, the average fasting and postprandial plasma glucose levels decreased by 49.3% and 42.7%, respectively. LL-2113AD was also well tolerated and no serious adverse events or side effects were reported (72). LL-2113AD is available from Lupin.

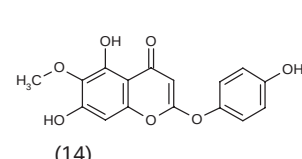
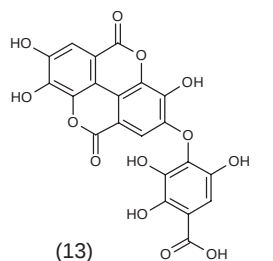
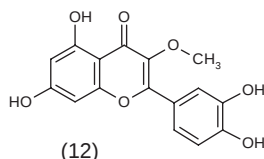
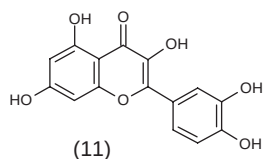
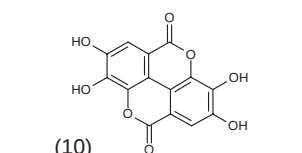
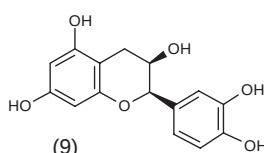
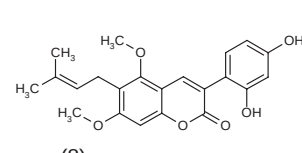
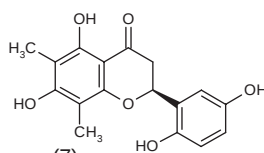
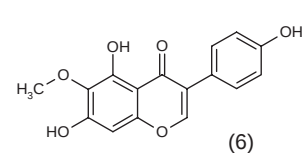
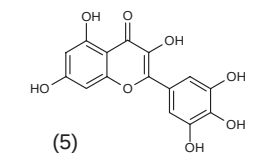
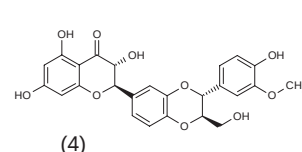
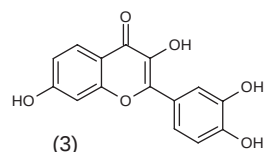
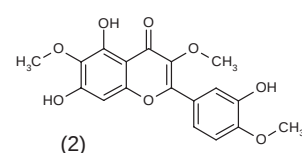
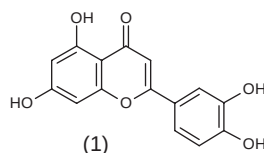
ID-1101 (4-hydroxyisoleucine), an amino acid extracted from fenugreek seeds, has demonstrated insulinotropic effects in the rat and improvements in insulin sensitivity (73). Innodia has reported the completion of a phase Ia trial that indicated that ID-1101 given orally as escalating single doses was well tolerated, with an excellent safety profile and dose-proportional pharmacokinetics. Regulatory approval from Health Canada was recently granted to Innodia to commence a multiple-dose phase Ib trial with ID-1101 (74).

At present, a natural substitute for insulin seems unlikely, although traditional phytotherapies may provide valuable clues for the development of new oral hypoglycemic agents and simple dietary adjuncts. Antidiabetic products originating from natural sources are indexed in Tables I and II.

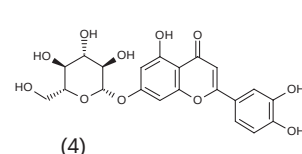
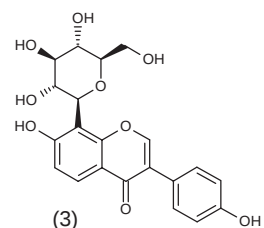
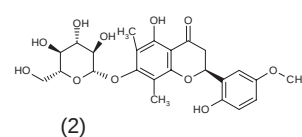
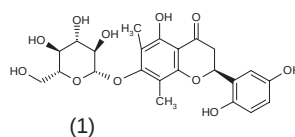
Table I: Chemical structures of active antidiabetic constituents from plants (from Prous Science Integrity®).

Flavonoids

1. Luteolin
Brassica oleracea var. *italica*
Lactuca indica
2. Centaureidin
Cynara scolymus L.
Brickellia veronicifolia
Tanacetum parthenium
3. Fisetin
Toxicodendron vernicifluum
4. Silibinin
Silybum marianum
5. Myricetin
Morella rubra
Camellia sinensis
6. Tectorigenin
Belamcanda chinensis
Pueraria montana
7. Myricacetin
Myrcia multiflora DC
8. Glycyrrin
Glycyrrhiza uralensis
9. Epicatechin
Pterocarpus marsupium Roxb.
Camellia sinensis
Waltheria indica
10. Ellagic acid
Vitis vinifera L.
Phyllanthus urinaria
11. Quercetin
Hypericum perforatum
Ficus racemosa L.
Oryza sativa L.
Euphorbia lunulata
Waltheria indica
Phellodendron japonicum
Opuntia ficus-indica
Opuntia ficus-indica
Cistus laurifolius
Caesalpinia ferrea
12. Quercetin-3-O-methyl ether
Artemisia capillaris

**Glycoside-Flavonoids**

1. Myricitrin I
Myrcia multiflora DC
2. Myricitrin II
Myrcia multiflora DC
3. Puerarin
Pueraria montana
Angelica keiskei koizumi
Carthamus tinctorius
Cynara scolymus L.
Firmiana simplex
Lactuca indica
Olea europaea
4. Cynaroside

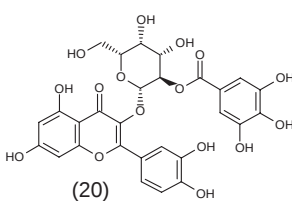
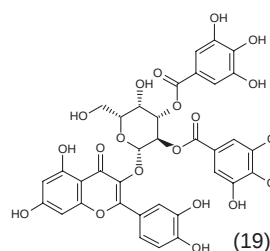
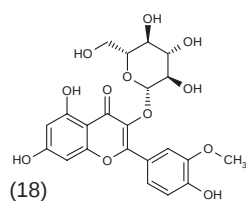
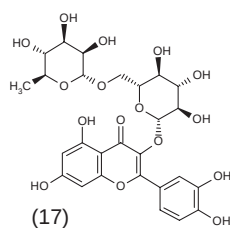
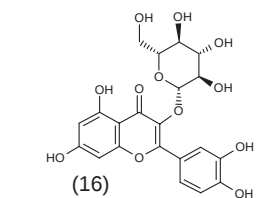
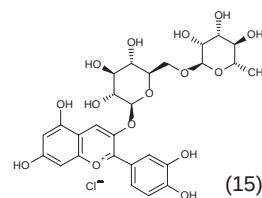
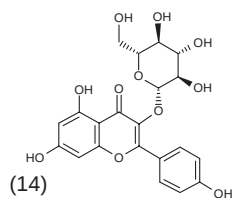
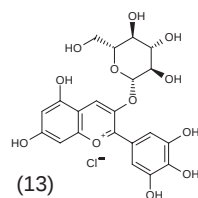
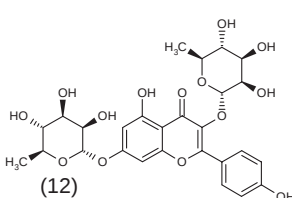
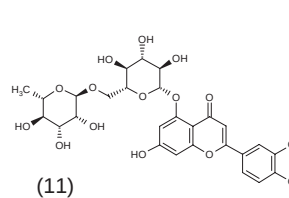
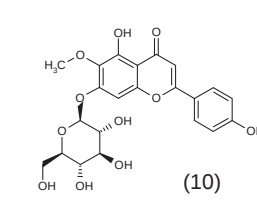
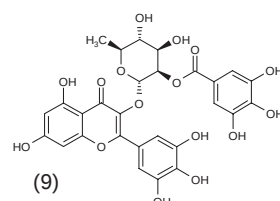
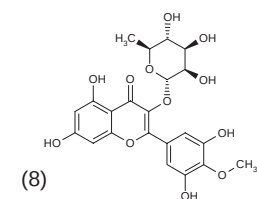
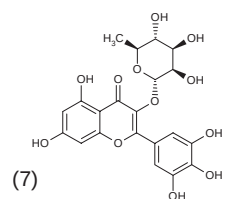
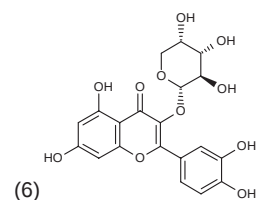
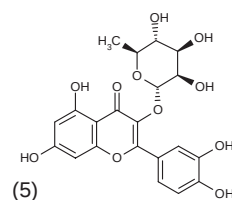


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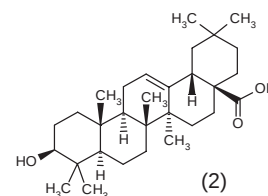
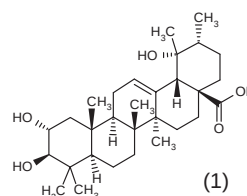
Table I: Chemical structures of active antidiabetic constituents from plants (from Prous Science Integrity®).

Glycoside-Flavonoids

- | | |
|---|------------------------------------|
| 5. Quercitrin | <i>Hypericum perforatum</i> |
| 6. Guaijaverin | <i>Myrcia multiflora</i> DC |
| 7. Myricitrin | <i>Myrcia multiflora</i> DC |
| | <i>Morella rubra</i> |
| 8. Mearncitrin | <i>Myrcia multiflora</i> DC |
| 9. Desmanthin-1 | <i>Myrcia multiflora</i> DC |
| 10. Tectoridin | <i>Pueraria montana</i> |
| 11. Luteolin-5-O- β -rutinoside | <i>Salvia lavandulifolia</i> Vahl |
| 12. Kaempferitrin | <i>Bauhinia forficata</i> |
| | <i>Cinnamomum osmophloeum</i> |
| 13. Myrtillin | <i>Hibiscus sabdariffa</i> |
| | <i>Vaccinium myrtillus</i> |
| | <i>Glycine max</i> |
| 14. Astragalin | <i>Eucommia ulmoides</i> |
| | <i>Crassocephalum crepidioides</i> |
| | <i>Diospyros cathayensis</i> |
| 15. Antirrhinin | <i>Prunus cerasus</i> |
| | <i>Ribes nigrum</i> |
| | <i>Rubus idaeus</i> |
| 16. Isoquercitrin | <i>Sedum sarmentosum</i> |
| | <i>Diospyros kaki</i> |
| | <i>Crassocephalum crepidioides</i> |
| | <i>Diospyros cathayensis</i> |
| | <i>Vicia monantha</i> |
| 17. Rutin | <i>Vicia monantha</i> |
| 18. Isorhamnetin-3-O- β -D-glucopyranoside | <i>Descurainia sophia</i> |
| 19. Quercetin 3-O-(2'',3''-digalloyl)- β -D-galactopyranoside | <i>Euphorbia lunulata</i> |
| 20. Quercetin 3-O-(2''-galloyl)- β -D-galactopyranoside | <i>Euphorbia lunulata</i> |

**Terpenoids**

- | | |
|-------------------|---------------------------------|
| 1. Tormentic acid | <i>Sanguisorba ancistroides</i> |
| 2. Oleanolic acid | <i>Vitis vinifera</i> L. |
| | <i>Catharanthus roseus</i> |
| | <i>Bassia scoparia</i> |
| | <i>Olea europaea</i> |
| | <i>Dracocephalum kotschy</i> |

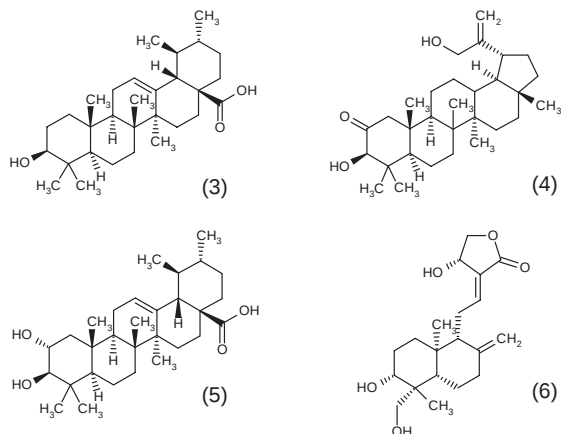


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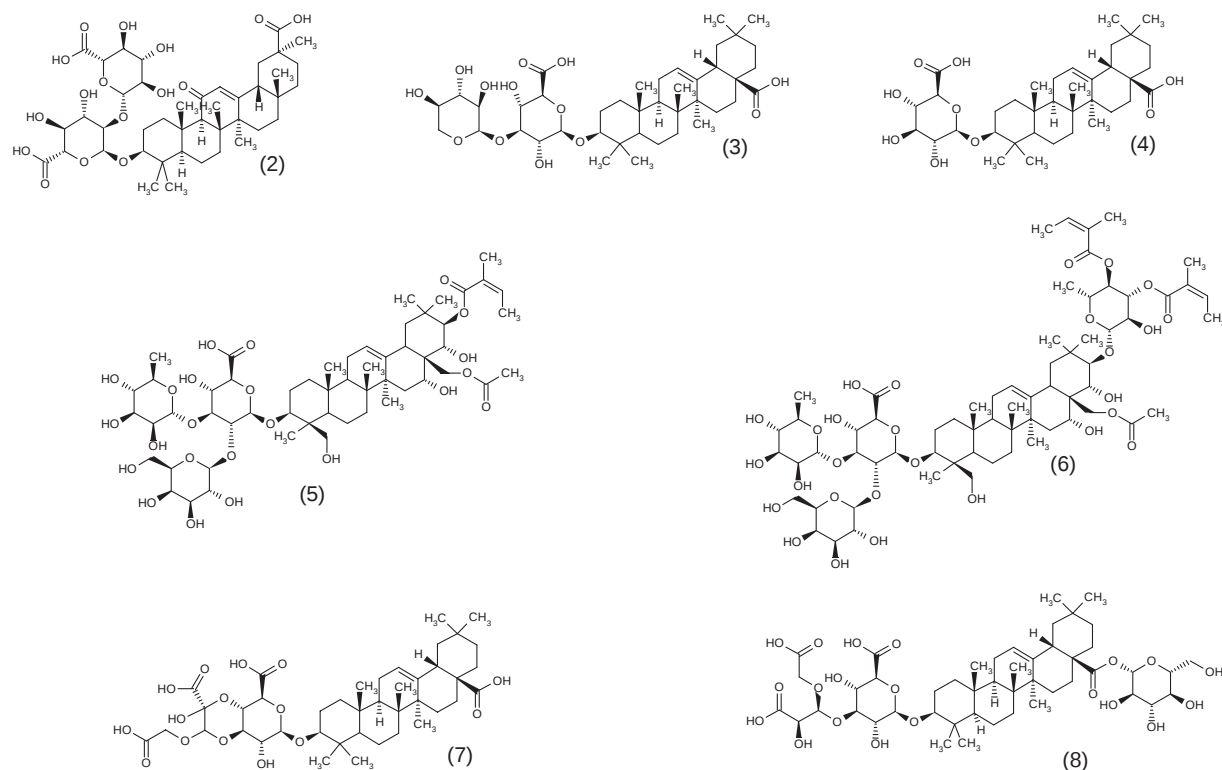
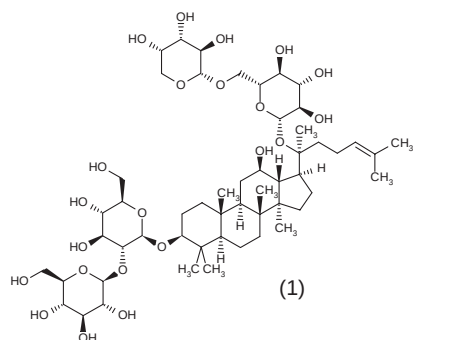
Table I: Chemical structures of active antidiabetic constituents from plants (from Prous Science Integrity®).

Terpenoids

- | | |
|---|---|
| 3. Ursolic acid | <i>Catharanthus roseus</i>
<i>Coridothymus capitatus</i>
<i>Dracocephalum kotschy</i>
<i>Centella asiatica</i>
<i>Salacia chinensis</i> |
| 4. 3 β ,29-Dihydroxylup-20(30)-en-2-one | |
| 5. Corosolic acid | <i>Pseudocymodonia sinensis</i>
<i>Lagerstroemia speciosa</i> (L.) Pers.
<i>Dracocephalum kotschy</i>
<i>Eriobotrya japonica</i>
<i>Centella asiatica</i> |
| 6. Andrographolide | <i>Andrographis paniculata</i> |

**Glycoside-terpenoids**

- | | |
|------------------------|---------------------------------|
| 1. Ginsenoside Rb2 | <i>Panax ginseng</i> C.A. Meyer |
| 2. Glycyrrhizin | <i>Glycyrrhiza glabra</i> |
| 3. Momordin Ic | <i>Bassia scoparia</i> |
| 4. Momordin Ib | <i>Aralia elata</i> Seem. |
| 5. Assamicin I | <i>Aesculus assamica</i> Griff |
| 6. Assamicin II | <i>Aesculus assamica</i> Griff |
| 7. Betavulgaroside II | <i>Beta vulgaris</i> L. |
| 8. Betavulgaroside III | <i>Beta vulgaris</i> L. |

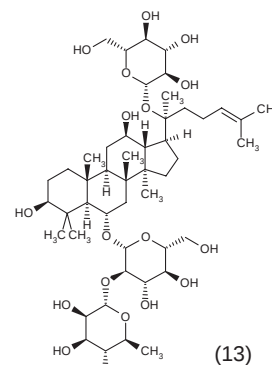
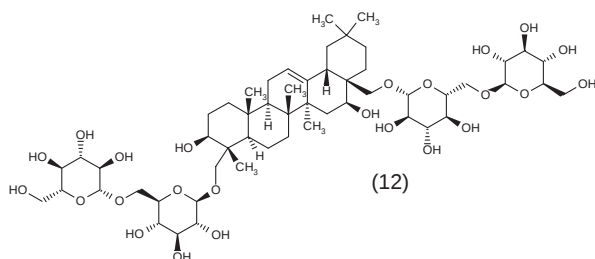
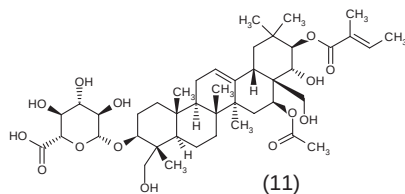
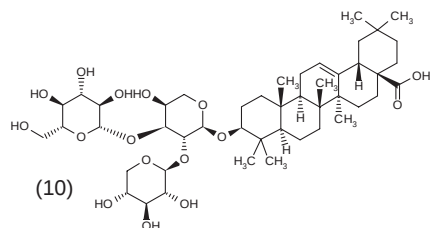
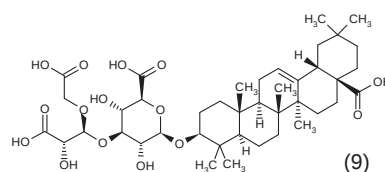


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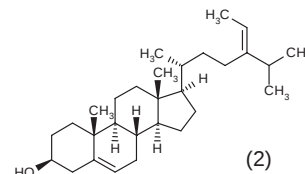
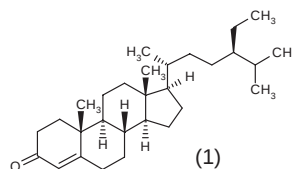
Table I: Chemical structures of active antidiabetic constituents from plants (from Prous Science Integrity®).

Glycoside-terpenoids

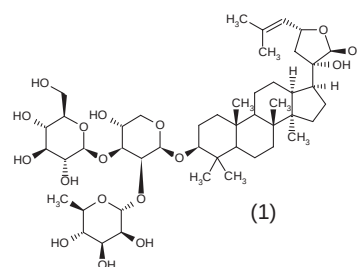
- | | |
|-----------------------|---------------------------------|
| 9. Betavulgaroside IV | <i>Beta vulgaris</i> L. |
| 10. Elatoside E | <i>Aralia elata</i> Seem. |
| 11. Gymnemoside B | <i>Gymnema sylvestre</i> |
| 12. Gymnemasaponin V | <i>Gymnema sylvestre</i> |
| 13. Ginsenoside Re | <i>Panax ginseng</i> C.A. Meyer |

**Steroids**

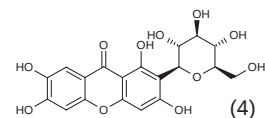
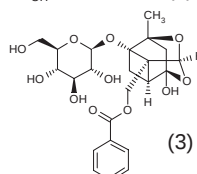
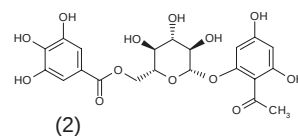
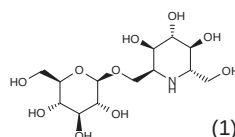
- | | |
|-----------------------|----------------------------------|
| 1. 4-Stigmasten-3-one | <i>Salvia amplexicaulis</i> Lam. |
| 2. Fucosterol | <i>Silvestia siliquosa</i> |

**Glycoside-steroids**

- | | |
|--------------|--------------------------------|
| 1. Phanoside | <i>Gynostemma pentaphyllum</i> |
|--------------|--------------------------------|

**Glycosides**

- | | |
|--------------------|----------------------------------|
| 1. MDL-25637 | <i>Hyacinthus orientalis</i> |
| 2. Myrciaphenone B | <i>Lobelia sessilifolia</i> |
| 3. Paeoniflorin | <i>Myrcia multiflora</i> DC |
| 4. Mangiferin | <i>Paeonia lactiflora</i> |
| | <i>Anemarrhena asphodeloides</i> |

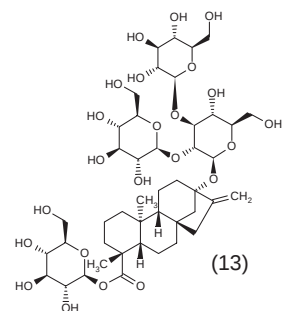
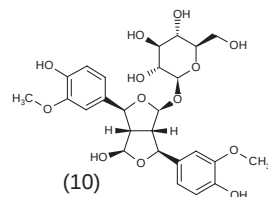
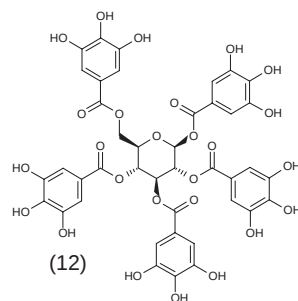
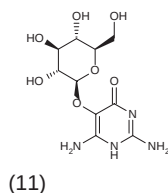
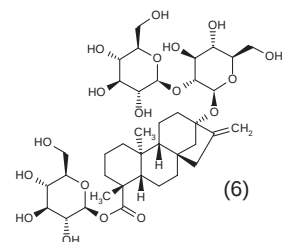
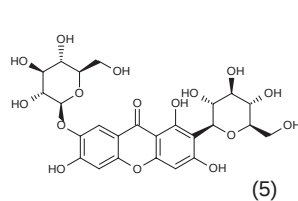
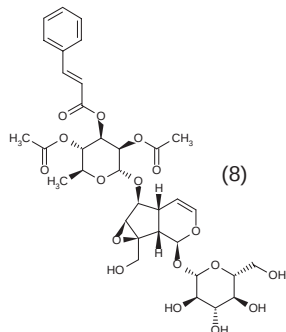
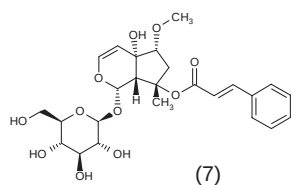


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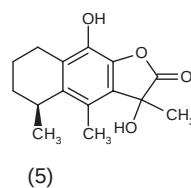
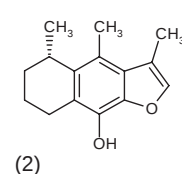
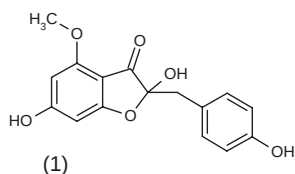
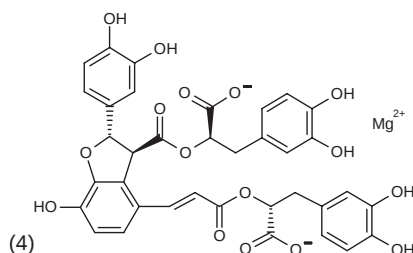
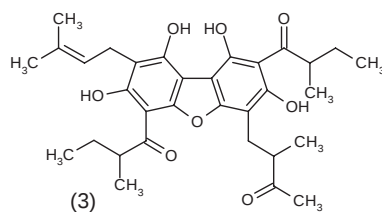
Table I: Chemical structures of active antidiabetic constituents from plants (from Prous Science Integrity®).

Glycosides

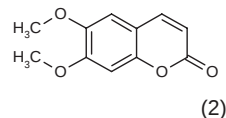
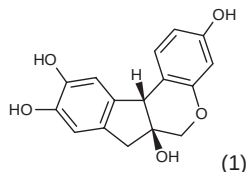
- | | |
|--------------------------|----------------------------------|
| 5. Neomangiferin | <i>Anemarrhena asphodeloides</i> |
| 6. Stevioside | <i>Stevia rebaudiana</i> Berton |
| 7. Harpagoside B | <i>Scrophularia deserti</i> |
| 8. Scropolioside D | <i>Scrophularia deserti</i> |
| 9. Kotalanol | <i>Salacia oblonga</i> Wall |
| | <i>Salacia reticulata</i> Wight |
| 10. Lactucaside | <i>Lactuca indica</i> |
| 11. Vicine | <i>Momordica charantia</i> |
| 12. Pentagalloyl glucose | <i>Pelargonium inquinans</i> |
| 13. Rebaudioside A | <i>Stevia rebaudiana</i> Berton |

**Benzofuranes**

- | | |
|------------------------------|------------------------------------|
| 1. Marsupin | <i>Pterocarpus marsupium</i> Roxb. |
| 2. Cacalol | <i>Psacalium decompositum</i> |
| 3. Achyrofuran | <i>Achyrocline satureioides</i> |
| 4. Magnesium lithospermate B | <i>Salvia miltiorrhiza</i> |
| 5. 245951 | <i>Psacalium decompositum</i> |

**Benzopyranes**

- | | |
|--------------|------------------------------|
| 1. Brazilin | <i>Caesalpinia sappan</i> L. |
| 2. Scoparone | <i>Artemisia capillaris</i> |

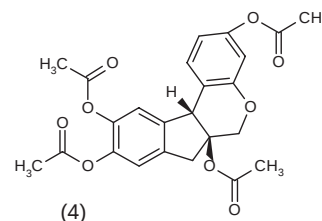
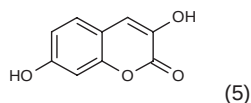
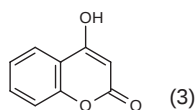


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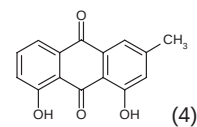
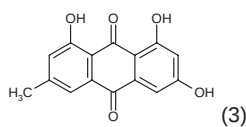
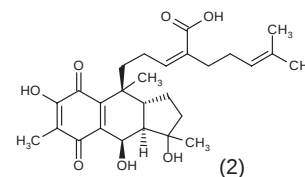
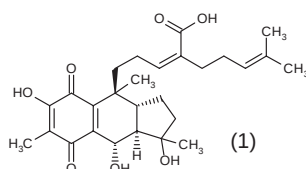
Table I: Chemical structures of active antidiabetic constituents from plants (from Prous Science Integrity®).

Benzopyranes

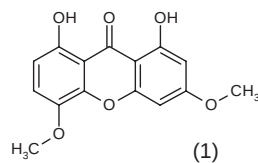
- | | |
|--------------------------|------------------------------|
| 3. 4-Monohydroxycoumarin | <i>Artemisia capillaris</i> |
| 4. Tetraacetylbraziin | <i>Caesalpinia sappan</i> L. |
| 5. 3,7-Dihydroxycoumarin | <i>Euphorbia terracina</i> |

**Quinones**

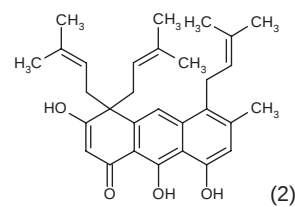
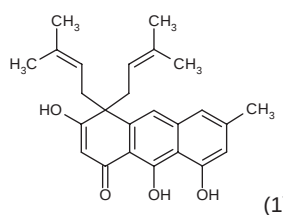
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|-----------------------|------------------------------|
| 1. Pycnanthuquinone B | <i>Pycnanthus angolensis</i> |
| 2. Pycnanthuquinone A | <i>Pycnanthus angolensis</i> |
| 3. Emodin | <i>Rheum undulatum</i> |
| | <i>Rheum officinale</i> |
| 4. Chrysophanol | <i>Rheum undulatum</i> |

**Xanthones**

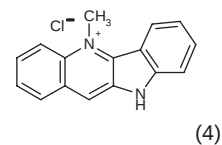
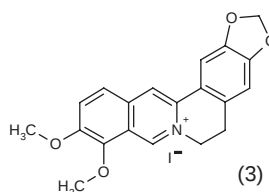
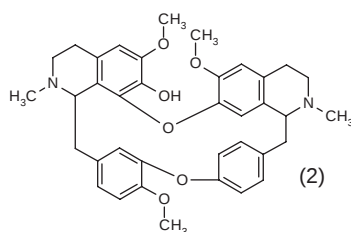
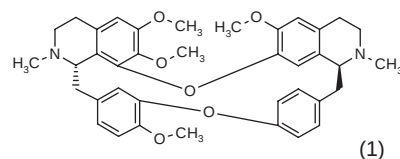
- | | |
|---------------|--------------------------|
| 1. Swerchirin | <i>Swertia chirayita</i> |
|---------------|--------------------------|

**Anthracenes**

- | | |
|---------------|-----------------------------------|
| 1. Vismin | <i>Harungana madagascariensis</i> |
| 2. Harunganin | <i>Harungana madagascariensis</i> |

**Alkaloids**

- | | |
|--------------------------|-------------------------------------|
| 1. Tetrandrine | <i>Stephania tetrandra</i> S. Moore |
| 2. Fangchinoline | <i>Stephania tetrandra</i> S. Moore |
| 3. Berberine iodide | <i>Coptis chinensis</i> |
| 4. Cryptolepine chloride | <i>Cryptolepis sanguinolenta</i> |

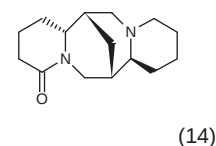
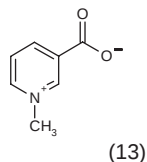
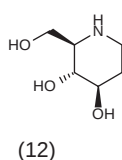
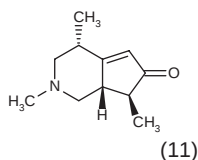
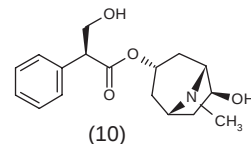
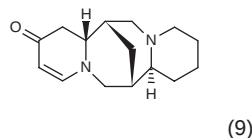
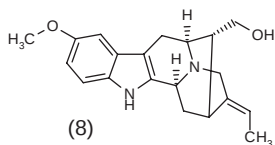
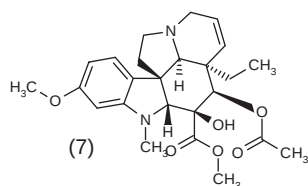


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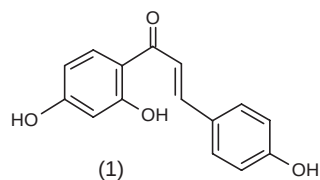
Table I: Chemical structures of active antidiabetic constituents from plants (from Prous Science Integrity®).

Alkaloids

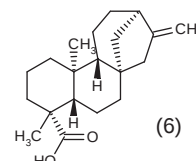
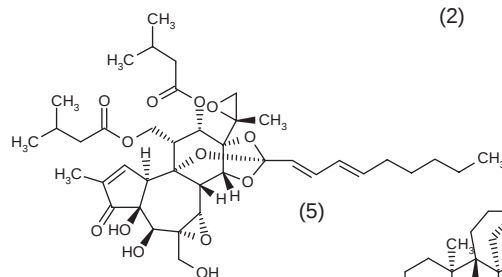
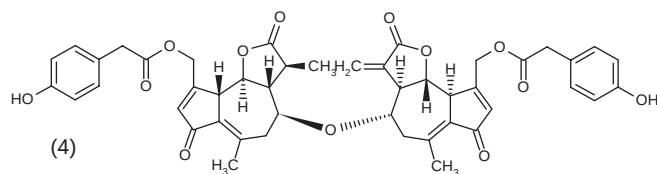
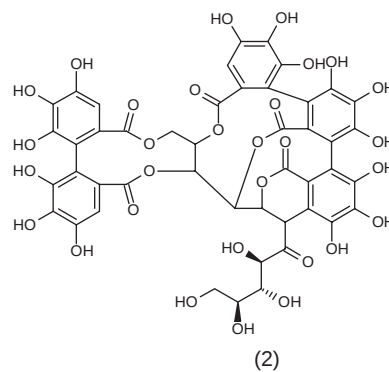
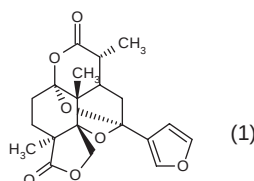
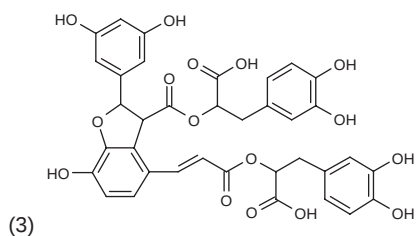
- | | |
|------------------------|--|
| 5. Tetrahydroalstonine | <i>Catharanthus roseus</i> |
| 6. Vindolinine | <i>Catharanthus roseus</i> |
| 7. Vindoline | <i>Catharanthus roseus</i> |
| 8. Lochnerine | <i>Catharanthus roseus</i> |
| 9. Multiflorine | <i>Lupinus pilosus</i> |
| 10. Anisodamine | <i>Anisodis tanguticus</i> |
| 11. Tecomanine | <i>Tecoma stans</i> |
| 12. Fagomine | <i>Morus alba</i> |
| 13. Trigonelline | <i>Trigonella foenum-graecum</i> |
| 14. Lupanine | <i>Lupinus albus</i> var. <i>albus</i> |

**Chalcones**

- | | |
|----------------------|------------------------------|
| 1. Isoliquiritigenin | <i>Glycyrrhiza uralensis</i> |
|----------------------|------------------------------|

**Polycyclics**

- | | |
|-------------------|-----------------------------------|
| 1. Saudin | <i>Cluytia richardiana</i> |
| 2. Grandinin | <i>Melaleuca quinquenervia</i> |
| 3. Lithosperman B | <i>Lithospermum erythrorhizon</i> |
| 4. Lactucain C | <i>Lactuca indica</i> |
| 5. Maprouneacin | <i>Maprounea africana</i> |
| 6. Kaurenoic acid | <i>Aralia cordata</i> |
| | <i>Mikania glomerata</i> |

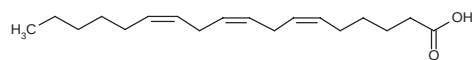


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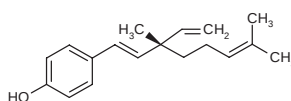
Table I: Chemical structures of active antidiabetic constituents from plants (from Prous Science Integrity®).

Miscellaneous

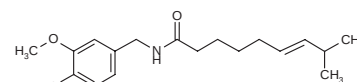
1. Gamolenic acid *Borago officinalis*
2. Bakuchiol *Cullen corylifolium*
Otholobium pubescens
Otholobium glandulosum
3. Capsaicin *Capsicum frutescens*
4. Pinitol *Bougainvillea spectabilis*
Pinus halepensis Mill.
Pinus lambertiana Douglas
Pinus sylvestris
5. Salacinol *Salacia oblonga* Wall
Salacia reticulata Wight
6. Isoferulic acid *Actaea dahurica*
Actaea heracleifolia
Actaea racemosa L.
7. 4-HBA *Pandanus amaryllifolius*
8. Cinnamaldehyde *Cinnamomum aromaticum* Nees
9. Pterostilbene *Pterocarpus marsupium* Roxb.
10. Meglutol *Tillandsia usneoides*
11. ID-1101 *Trigonella foenum-graecum*
12. MCPG *Litchi chinensis*
13. Alliin *Allium sativum*
14. Allicin *Allium sativum*
15. Deoxyrhapontigenin *Rheum undulatum*
16. Apocynin *Paeonia suffruticosa*
17. APDS *Allium sativum*
Allium cepa
18. 3,4,5-Tricaffeoylquinic acid *Ipomoea batatas*
19. Reticulanol *Salacia reticulata* Wight
20. *p*-Methoxycinnamic acid *Oryza sativa* L.
Scrophularia buergeriana
21. Bilobol dimethyl ether *Ginkgo biloba*
22. Gallic acid *Paeonia lactiflora*
Euphorbia lunulata
Rubus suavissimus



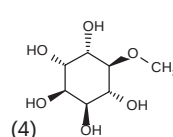
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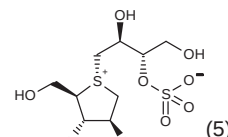
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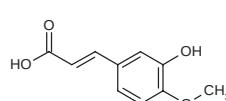
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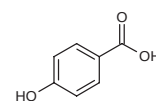
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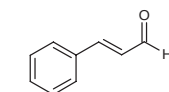
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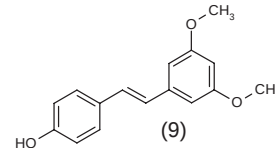
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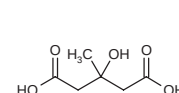
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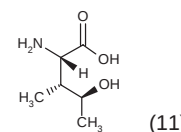
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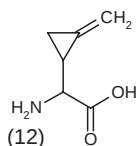
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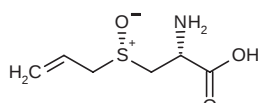
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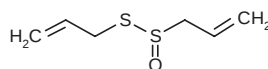
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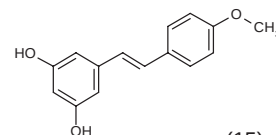
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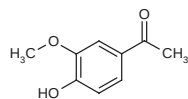
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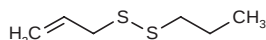
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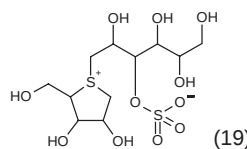
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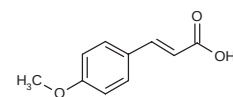
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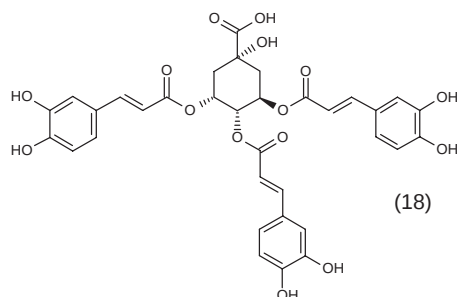
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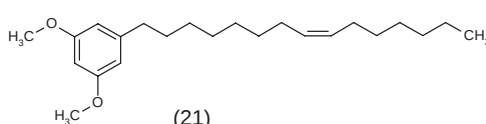
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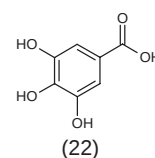
(19)



(20)



(21)



(22)

(Continuation)

Table I: Chemical structures of active antidiabetic constituents from plants (from Prous Science Integrity®).

Structure not yet determined:

Polysaccharides

1. Moran A	<i>Morus alba</i>
2. Aconitan A	<i>Aconitum carmichaelii</i>
3. Aconitan B	<i>Aconitum carmichaelii</i>
4. Aconitan C	<i>Aconitum carmichaelii</i>
5. Coixan A	<i>Coix lacryma-jobi</i> L.
6. Ganoderan A	<i>Ganoderma lucidum</i>
7. Ganoderan B	<i>Ganoderma lucidum</i>
8. Atractan A	<i>Atractylodes japonica</i>
9. Atractan B	<i>Atractylodes japonica</i>
10. Atractan C	<i>Atractylodes japonica</i>
11. Dioscoran A	<i>Dioscorea japonica</i>
12. Dioscoran B	<i>Dioscorea japonica</i>
13. Dioscoran C	<i>Dioscorea japonica</i>
14. Dioscoran D	<i>Dioscorea japonica</i>
15. Dioscoran E	<i>Dioscorea japonica</i>
16. Dioscoran F	<i>Dioscorea japonica</i>
17. Lithosperman A	<i>Lithospermum erythrorhizon</i>
18. Lithosperman C	<i>Lithospermum erythrorhizon</i>
19. Quinquefolan A	<i>Panax quinquefolius</i> L.
20. Trichosan A	<i>Trichosanthes kirilowii</i> Maxim.
21. Panaxan A	<i>Panax ginseng</i> C.A. Meyer
22. Panaxan B	<i>Panax ginseng</i> C.A. Meyer
23. Ephedran A	<i>Ephedra distachya</i> L.
24. Ephedran B	<i>Ephedra distachya</i> L.
25. Ephedran C	<i>Ephedra distachya</i> L.
26. Ephedran D	<i>Ephedra distachya</i> L.
27. Ephedran E	<i>Ephedra distachya</i> L.
28. Eleutheran A	<i>Eleutherococcus senticosus</i>
29. Eleutheran B	<i>Eleutherococcus senticosus</i>
30. Eleutheran C	<i>Eleutherococcus senticosus</i>
31. Eleutheran D	<i>Eleutherococcus senticosus</i>
32. Eleutheran E	<i>Eleutherococcus senticosus</i>
33. Eleutheran F	<i>Eleutherococcus senticosus</i>
34. Eleutheran G	<i>Eleutherococcus senticosus</i>
35. Oryzabran A	<i>Oryza sativa</i> L.
36. Oryzabran B	<i>Oryza sativa</i> L.
37. Oryzabran C	<i>Oryza sativa</i> L.
38. Oryzabran D	<i>Oryza sativa</i> L.
39. Oryzaran A	<i>Oryza sativa</i> L.
40. Oryzaran B	<i>Oryza sativa</i> L.
41. Oryzaran C	<i>Oryza sativa</i> L.
42. Oryzaran D	<i>Oryza sativa</i> L.
43. Glucomannan	<i>Aloe vera</i> <i>Amorphophallus konjac</i>

Peptides

1. Charantin	<i>Momordica charantia</i>
2. Polypeptide-P	<i>Momordica charantia</i>

Glycoside-terpenoids

1. Gymnemic acids	<i>Gymnema sylvestre</i>
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Table II: Natural sources of antidiabetic constituents (from Prous Science Integrity®).

Plant	Product	Ref.
<i>Acer pseudoplatanus</i> L.	MCPG	75,76
<i>Achyrocline satureioides</i>	Achyrofuran	77
<i>Aconitum carmichaelii</i>	Aconitan A	55,78-81
<i>Actaea dahurica</i> (<i>Cimicifuga dahurica</i>)	Isoferulic acid	82-85
<i>Actaea heracleifolia</i> (<i>Cimicifuga heracleifolia</i>)	Isoferulic acid	82-85
<i>Actaea racemosa</i> L. (<i>Cimicifuga racemosa</i>)	Isoferulic acid	82-85
<i>Aesculus assamica</i> Griff	Assamicin I	86
	Assamicin II	86
<i>Allium cepa</i>	APDS	9,75,87,88
<i>Allium sativum</i>	APDS	9,75,87,88
	Alliin	10,89
<i>Aloe vera</i>	<i>Aloe vera</i> gel	11,13,14,90-92,94,95,97
	Glucomannan	93,96,98,103,104
<i>Amorphophallus konjac</i>	Glucomannan	93,96,98,103,104
<i>Andrographis paniculata</i>	Andrographolide	105,106
<i>Anemarrhena asphodeloides</i>	Mangiferin	107-111
	Neomangiferin	107,109,111
<i>Angelica keiskei</i> koizumi	Cynarside	112,113,422
<i>Anisodus tanguticus</i>	Anisodamine	75
<i>Aralia cordata</i>	Kaurenoic acid	114
<i>Aralia elata</i> Seem.	Momordin Ib	115,116,119,123,124
	Elatoside E	115,119,120,123,124
	Oleanolic acid 3-O-glucuronide	120
<i>Artemisia capillaris</i>	4-Monohydroxycoumarin	125,126
	Capillarisin	125,126
	Scoparone	126
<i>Artemisia dracunculus</i>	<i>Artemisia dracunculus</i> extract	127,128
<i>Atractylodes japonica</i>	Atractan A	75,129
	Atractan B	75,129
	Atractan C	75,129
<i>Avena sativa</i>	Oat beta-glucan	50,130-135
<i>Bassia scoparia</i> (<i>Kochia scoparia</i>)	Momordin Ic	117,119,120,137
	Oleanolic acid	136
<i>Bauhinia forficata</i>	Kaempferitrin	138,139
<i>Belamcanda chinensis</i>	Tectorigenin	140
<i>Berberis aristata</i>	Berberine iodide	55,141-144
<i>Beta vulgaris</i> L.	Betavulgaroside II	145,146
	Betavulgaroside III	145-147
	Betavulgaroside IV	145-147
<i>Bombax ceiba</i>	Mangiferin	107-111
<i>Borago officinalis</i>	Gamolenic acid	58,148-166,423,424
<i>Bougainvillea spectabilis</i>	Pinitol	167-171,425
<i>Brassica oleracea</i> var. <i>italica</i>	Luteolin	172
<i>Brickellia veronicifolia</i>	Centaureidin	173
<i>Caesalpinia bonduc</i> (<i>C. bonducella</i>)	BM-169	174
<i>Caesalpinia ferrea</i>	2-(2,3,6-Trihydroxy-4-carboxyphenyl)ellagic acid	426,427
	BM-170B	174
<i>Caesalpinia sappan</i> L.	Tetraacetylbrazililn	175
	Brazilin	75,176-180
<i>Camellia sinensis</i>	Myricetin	181,183,184,443
	Oolong tea	182,185
	Epicatechin	186-189
<i>Cannabis sativa</i>	<i>Cannabis sativa</i> L. extract	190
<i>Capsicum frutescens</i>	Capsaicin	191-198
<i>Carthamus tinctorius</i>	Cynarside	112,113,422
<i>Catharanthus roseus</i> (<i>Vinca rosea</i>)	Oleanolic acid	136
	Vindolinine	5,199
	Vindoline	5,199
	Lochnerine	5,199

(Continuation)

Table II: Natural sources of antidiabetic constituents (from Prous Science Integrity®).

Plant	Product	Ref.
<i>Catharanthus roseus</i> (<i>Vinca rosea</i>)	Tetrahydroalstonine	200
	Ursolic acid	75,201
<i>Centella asiatica</i>	Ursolic acid	75,201
	Total triterpenic fraction of <i>Centella asiatica</i>	202,203
	Corosolic acid	204,205,428,429
<i>Cinnamomum aromaticum</i> Nees (<i>Cinnamomum cassia</i>)	Cinnamon extract	206,207
<i>Cinnamomum osmophloeum</i>	Kaempferitrin	138,139
<i>Cistus laurifolius</i>	Quercetin-3-O-methyl ether	431
<i>Cluytia richardiana</i>	Saudin	432
<i>Coccinia grandis</i> (<i>C. indica</i>)	<i>Coccinia indica</i> extract	208-213
<i>Coix lacryma-jobi</i> L.	Coixan A	214
<i>Coptis chinensis</i>	Berberine iodide	55,141-144
<i>Coridothymus capitatus</i>	Ursolic acid	75,201
<i>Crassocephalum crepidioides</i>	Isoquercitrin	215
	Astragalin	433
<i>Cryptolepis sanguinolenta</i>	Cryptolepine chloride	216-219,434,435
<i>Cucurbita ficifolia</i>	<i>Cucurbita ficifolia</i> extract	220
<i>Cullen corylifolium</i> (<i>Psoralea corylifolia</i>)	Bakuchiol	221
<i>Curcuma longa</i>	Turmeric extract	222,223
	Curcumin	223
<i>Cynara scolymus</i> L.	Cynaroside	112,113,422
	Luteolin	172
<i>Descurainia sophia</i>	Isorhamnetin-3-O- β -D-glucopyranoside	224
<i>Dioscorea japonica</i>	Dioscoran A	225
	Dioscoran B	225
	Dioscoran C	225
	Dioscoran D	225
	Dioscoran E	225
	Dioscoran F	225
<i>Diospyros cathayensis</i>	Isoquercitrin	215
	Astragalin	433
<i>Diospyros kaki</i>	Isoquercitrin	215
<i>Dipteryx odorata</i>	Isoliquiritigenin	226,227
<i>Dracocephalum kotschy</i>	Ursolic acid	75,201
	Corosolic acid	204,205,428,429
	Oleanolic acid	136
<i>Eleutherococcus senticosus</i> (<i>Acanthopanax senticosus</i>)	Eleutheran A	228
	Eleutheran B	228
	Eleutheran C	228
	Eleutheran D	228
	Eleutheran E	228
	Eleutheran F	228
	Eleutheran G	228
<i>Enicostemma littorale</i>	<i>Enicostemma littorale</i> extract	229,232
<i>Ephedra distachya</i> L.	Ephedran A	75,233
	Ephedran B	75,233
	Ephedran C	75,233
	Ephedran D	75,233
	Ephedran E	75,233
<i>Equisetum myriochaetum</i>	<i>Equisetum myriochaetum</i> extract	235,236
<i>Eriobotrya japonica</i>	Corosolic acid	204,205,428,429
<i>Eucommia ulmoides</i>	Astragalin	433
<i>Euphorbia lunulata</i>	Quercetin	181,237-240,242,244,422,436
	Gallic acid	241,243
	Quercetin 3-O-(2",3"-digalloyl)- β -D-galactopyranoside	437
	Quercetin 3-O-(2"-galloyl)- β -D-galactopyranoside	437
<i>Euphorbia terracina</i>	3,7-Dihydroxycoumarin	438,439

(Continuation)

Table II: Natural sources of antidiabetic constituents (from Prous Science Integrity®).

Plant	Product	Ref.
<i>Ficus racemosa</i> L.	Quercetin	181,237-240,242,244,422,436
<i>Firmiana simplex</i>	Quercitrin	113,422,443
<i>Fumaria parviflora</i>	<i>Fumaria parviflora</i> extract	245
<i>Ganoderma lucidum</i>	Ganoderan B	79,246-248
<i>Ginkgo biloba</i>	<i>Ginkgo biloba</i> extract	249-262
	Bilobol dimethyl ether	440
<i>Glycine max</i>	Touchi extract	263,264
	Myrtillin	265
<i>Glycyrrhiza glabra</i>	Glycyrrhizin	266-270
<i>Glycyrrhiza uralensis</i>	Isoliquiritigenin	226,227
	Glycyrin	271,272
<i>Gmelina asiatica</i>	<i>Gmelina asiatica</i> extract	273
<i>Gymnema sylvestre</i>	<i>Gymnema sylvestre</i> extract	11,75,274-281,411
	Gymnemoside B	75,278,279,281
	Gymnemasaponin V	75,278,279
	Gymnemic acids	17,276,279-281,412
<i>Gynostemma pentaphyllum</i>	Phanoside	282,283
<i>Harungana madagascariensis</i>	Vismin	441
	Harunganin	441,442
<i>Hibiscus sabdariffa</i>	Myrtillin	265
<i>Hordeum vulgare</i>	Young barley leaf extract	265
<i>Hyacinthus orientalis</i>	MDL-25637	285-289
<i>Hydrastis canadensis</i>	Berberine iodide	55,141-144
<i>Hypericum perforatum</i>	Quercitrin	113,422,443
	Quercetin	181,237-240,242,244,422,436
<i>Ipomoea batatas</i>	<i>Ipomoea batatas</i> extract	70,71,290-292,413
	3,4,5-Tricaffeoylquinic acid	293
<i>Lactuca indica</i>	Cynaroside	112,113,422
	Luteolin	172
	Lactucain C	172
	Lactucaside	172
<i>Lagerstroemia speciosa</i> (L.) Pers.	Corosolic acid	204,205,428,429
<i>Lepidium didymum</i> (<i>Coronopus didymus</i>)	<i>Coronopus didymus</i> water extract	294
<i>Litchi chinensis</i>	MCPG	75,76
<i>Lithospermum erythrorhizon</i>	Lithosperman A	75,79,234
	Lithosperman B	75,79,234
	Lithosperman C	75,79,234
	MDL-25637	285-289
<i>Lobelia sessilifolia</i>	Lupanine	295
<i>Lupinus albus</i> var. <i>albus</i> (<i>Lupinus termis</i>)	Multiflorine	75,296
<i>Lupinus pilosus</i> (<i>Lupinus hirsutus</i>)	Berberine iodide	55,141-144
<i>Mahonia aquifolium</i>	Mangiferin	107-111
<i>Mangifera indica</i> L.	Maprouneacin	297
<i>Maprounea africana</i>	Grandinin	444
<i>Melaleuca quinquenervia</i>	Kaurenoic acid	114
<i>Mikania glomerata</i>	Polypeptide-P	15,75,90,298,300
<i>Momordica charantia</i>	Vicine	11,75,90
	<i>Momordica charantia</i> water extract	11,21,33,90,299,301-312,418
	Charantin	11,15,75,90,298
<i>Morella rubra</i> (<i>Myrica rubra</i>)	Myricetin	181,183,184,443
	Myricetin	445,446
<i>Morus alba</i>	Fagomine	313,314
	Moran A	315
<i>Mucuna pruriens</i>	<i>Mucuna pruriens</i> extract	306
<i>Muntingia calabura</i>	Isoliquiritigenin	226,227
<i>Myrcia multiflora</i> DC	Myrciacitrin I	118,121,443
	Myrciacitrin II	118,121
	Myrciaphenone B	118
	Mearncitrin	118
	Myrciacetin	118

(Continuation)

Table II: Natural sources of antidiabetic constituents (from Prous Science Integrity®).

Plant	Product	Ref.
<i>Myrcia multiflora</i> DC	Quercitrin	113,422,443
	Guaijaverin	113,118,443
	Desmanthin-1	113,118,443
	Myricitrin	445,446
<i>Nigella sativa</i>	<i>Nigella sativa</i> extract	316
Not determined	Kotalagenin 16-acetate	122
Not determined	α -Lipoic acid	149,155,317
Not determined	Oxylupanine	295
Not determined	17-Oxolupanine	295
Not determined	(+)-2-Thionosparteine	295
<i>Oenothera biennis</i>	Gamolenic acid	58,148-166
<i>Oenothera grandiflora</i> (<i>O. lamarckiana</i>)	Gamolenic acid	58,148-166
<i>Olea europaea</i>	Luteolin	172
	Cynaroside	112,113,422
	Oleanolic acid	136
<i>Opuntia ficus-indica</i>	Quercetin	181,237-240,242,244,422,436
	Quercetin-3-O-methyl ether	431
<i>Oryza sativa</i> L.	Quercetin	181,237-240,242,244,422,436
	Oryzabran A	318
	Oryzabran B	318
	Oryzabran C	318
	Oryzabran D	318
	Oryzaran A	414
	Oryzaran B	414
	Oryzaran C	414
	Oryzaran D	414
	p-Methoxycinnamic acid	319
<i>Otholobium glandulosum</i> (<i>Psoralea glandulosa</i>)	Bakuchiol	221
<i>Otholobium pubescens</i>	Bakuchiol	221
<i>Paeonia lactiflora</i>	Gallic acid	241,243
	Paeoniflorin	320,321
<i>Paeonia suffruticosa</i> (<i>P. moutan</i>)	Apocynin	322,323
<i>Panax ginseng</i> C. A. Meyer	Ginseng radix extract	324,415
	Ginsenoside Re	325
	Panaxan A	5,75,326-330
	Panaxan B	5,75,326-330
	Ginsenoside Rb2	447,448
<i>Panax quinquefolius</i> L.	North American ginseng extract	11,99-102,331
	Quinquefolan A	332
<i>Pandanus amaryllifolius</i> (<i>Pandanus odoratus</i>)	4-HBA	333,334
<i>Pelargonium inquinans</i>	Pentagalloyl glucose	449-451
<i>Phellodendron japonicum</i>	Scoparone	126
	Quercetin	181,237-240,242,244,422,436
<i>Phyllanthus amarus</i> (<i>Phyllanthus niruri</i>)	<i>Phyllanthus amarus</i> whole plant	416
<i>Phyllanthus urinaria</i>	Ellagic acid	427
<i>Pinus halepensis</i> Mill.	Pinitol	167-171,425
<i>Pinus lambertiana</i> Douglas	Pinitol	167-171,425
<i>Pinus pinaster</i>	Pycnogenol	317,335-338
<i>Pinus sylvestris</i>	Pinitol	167-171,425
<i>Plantago afra</i>	<i>Plantago Psyllium</i> mucilage	339
<i>Plantago ovata</i>	Psyllium	340-343
<i>Prunus cerasus</i>	Antirrhinin	344
<i>Psacalium decompositum</i>	Cacalol	345,346
	245951	441,442,452
<i>Pseudocydonia sinensis</i> (<i>Chaenomeles sinensis</i>)	Corosolic acid	204,205,428,429
	Tormentic acid	347
<i>Pterocarpus marsupium</i> Roxb.	Epicatechin	186-189
	Pterostilbene	5,350,352
	Marsupsin	5,350,352
	<i>Pterocarpus marsupium</i> extract	348,349,351

(Continuation)

Table II: Natural sources of antidiabetic constituents (from Prous Science Integrity®).

Plant	Product	Ref.
<i>Pterocarpus santalinus</i>	<i>Pterocarpus santalinus</i> water extract	419
<i>Pueraria montana</i> (<i>Pueraria thunbergiana</i>)	Tectorigenin	140
	Puerarin	69,353-356
	Tectoridin	445
<i>Punica granatum</i>	Gallic acid	241,243
<i>Pycnanthus angolensis</i>	Pycnanthuquinone A	197,357
	Pycnanthuquinone B	197,357,453
<i>Rehmannia glutinosa</i>	Rehmanniae Radix extract	358
<i>Rheum officinale</i>	Emodin	359,360
<i>Rheum undulatum</i>	Emodin	359,360
	Deoxyrhapontigenin	359
	Chrysophanol	359
<i>Ribes nigrum</i>	Antirrhinin	344
<i>Rosa rugosa</i>	Tormentic acid	347
<i>Rubus idaeus</i>	Antirrhinin	344
<i>Rubus suavissimus</i>	Gallic acid	241,243
<i>Salacia chinensis</i> (<i>Salacia prinosides</i>)	Mangiferin	107-111
	3 β ,29-Dihydroxylup-20(30)-en-2-one	454
<i>Salacia oblonga</i> Wall	Salacinol	113,122,362
	Kotalanol	113,122,361,362
<i>Salacia reticulata</i> Wight	Salacinol	113,122,362
	Kotalanol	113,122,361,362
	Mangiferin	107-111
	Reticulanol	455
<i>Salvia amplexicaulis</i> Lam.	4-Stigmasten-3-one	363,364
<i>Salvia lavandulifolia</i> Vahl	Luteolin-5-O- β -rutinoside	365
<i>Salvia miltiorrhiza</i>	Magnesium lithospermate B	366
<i>Sanguisorba ancistroides</i> (<i>Poterium ancistroides</i>)	Tormentic acid	347,429
<i>Scrophularia buergeriana</i>	p-Methoxycinnamic acid	319
<i>Scrophularia deserti</i>	Harpagoside B	367
	Scropolioside D	367
<i>Sedum sarmentosum</i>	Isoquercitrin	215
<i>Silvetia siliquosa</i> (<i>Pelvetia siliquosa</i>)	Fucosterol	456,457
<i>Silybum marianum</i> (<i>Carduus marianus</i>)	Silymarin	368,370,372
	Silibinin	369,371,417
<i>Stephania tetrandra</i> S. Moore	Tetrandrine	373-376
	Fangchinoline	458
<i>Stevia rebaudiana</i> Bertoni	Rebaudioside A	377,383
	Stevioside	378-383
<i>Swertia chirayita</i>	Swertichirin	75,384,385
	Mangiferin	107-111
<i>Syzygium cumini</i> (<i>Eugenia jambolana</i>)	<i>Eugenia jambolana</i> extract	386,387
	Gallic acid	241,243
<i>Tanacetum parthenium</i>	Centaureidin	173
<i>Tecoma stans</i>	Tecomanine	388-390
	Tecostanine	389
<i>Tillandsia usneoides</i>	Meglutol	391-393
<i>Toxicodendron vernicifluum</i> (<i>Rhus verniciflua</i>)	Fisetin	113,445
<i>Trichosanthes kirilowii</i> Maxim.	Tricosan A	394
<i>Trigonella foenum-graecum</i>	Fenugreek seed powder	90,351,395-400
	Trigonelline	75,402
	ID-1101	73,401,403-408,459,460
<i>Vaccinium myrtillus</i>	Myrtillin	265
	<i>Vaccinium myrtillus</i> anthocyanosides	409
<i>Vicia monantha</i> (<i>V. calcarata</i>)	Isoquercitrin	215
	Rutin	445
	Ellagic acid	427
<i>Vitis vinifera</i> L.	Oleanolic acid	136
<i>Waltheria indica</i>	Quercetin	181,237-240,242,244,422,436
	Epicatechin	186-189
<i>Xanthocercis zambesiaca</i>	Fagomine	313,314
<i>Zea mays</i> L.	<i>Zea mays</i> extract	410

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