Revista Brasileira de Farmacognosia
Brazilian Journal of Pharmacognosy
15(4): 392-413, Out./Dez. 2005
Received 08/22/05. Accepted 11/25/05

Revisão

Plants and their active constituents from South, Central, and North America with hypoglycemic activity

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ABSTRACT: There has been marked interest in recent years in the use of plants for the treatment of diabetes. Plants have been found in many countries which have been indicated as having hypoglycemic activity. The present work is an up-to-date review with 178 references of crude plant extracts and chemically defined molecules with hypoglycemic activity from South, Central and North America. The review refers to 224 plants with their families, parts used and type of extract, organism tested and activity. It also includes 40 compounds isolated from those plants. Some aspects of recent research with natural products from plants directed to the treatment of diabetes are discussed.

Keywords: Diabetes, hypoglycemic activity, medicinal plants, natural products.

INTRODUCTION

Diabetes is a disease in which the body does not produce insulin or use it properly. Insulin is a hormone needed to convert sugar, starch and other food into energy needed for daily life. The cause of diabetes continues to be a mystery, althought both genetic and environmental factors such as obesity and lack of exercise appear to play a part.

Worldwide 177 million people suffer from diabetes. This figure is likely to more than double by 2030 (See Table 1). The greater part of the increase is likely to occur in developing countries, which can least afford it.

The annual number of deaths in 2000 caused by diabetes mellitus in Latin America and the Caribbean has been estimated as 339035. This represents a loss of 757096 years of productive life among persons younger than 65 years (Barceló et al 2003). Diabetes is the third leading cause of death in the United States after heart disease and cancer (Acessed from http://www.medicinenet.com/Diabetes_Mellitus/article.htm in 01/21/2004).

Plants have always been an important source of drugs and many of the currently available drugs have been derived directly or indirectly from them. Ethnobotanical reports indicate about 1200 plants in the world with anti-diabetic potential (Alarcon-Aguilara et al 2002c), of which more than three hundred have been reported in the literature (Perez et al 1984; Almeida et al 1986; Bailey et al 1989; Handa et al 1989; Ivorra et al 1989; Oliveira et al 1989; Rahman et al 1989; Marles et al 1995; Ernest 1997; Pereira 1997; Perez et al 1998b; Volpato et al 2002; Grover et al 2002), referring to a large variety of identified chemical substances (Ivorra et al 1989; Rahman et al 1989; Marles et al 1995; Perez et al 1998b; Lamba et al 2000). The discovery of the widely used hypoglycemic drug, metformin (*N,N*-dimethylguanylguanidine) came from the traditional approach through the use of *Galega officinalis* (Grover et al 2002).

In a previous paper this research group has reviewed crude plant extracts and chemically defined molecules with potential antitumor activity for mammary (Moura et al 2001), cervical (Moura et al, 2002) and ovarian neoplasias (Silva et al 2003), as inhibitors of HMG CoA reductase (Gonçalves et al, 2000), central analgesic activity (Almeida et al, 2001), employed in prevention of osteoporosis (Pereira et al, 2002), for the treatment of Parkinson's disease (Morais, 2004) and antileishmanial activity (Rocha et al, 2005).

The present work reviews the literature on plants and plant-derived compounds from South, Central, and North America with hypoglycemic activity. Those plants which are used in the indigenous system of medicine have not been included, except for those whose hypoglycemic activity has been scientifically established.

The search was carred out on Chemical Abstracts, Biological Abstracts, Web of Sciences, LILACS (Latin American and Caribbean literature in Health Sciences) and the data bank of The University of Illinois in Chicago – NAPRALERT (Acronym for Natural Products ALERT), updated to December 2003, using hypoglycemic activity plus anti-diabetic as search terms. The references found in the search were consulted.

The search for data from different sources led

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ISSN 0102-695X

Table 1. Total of people with diabetes in some countries of South, Central and North America. (Accessed from http://www.int/ncd/dia/databases4.htmin on 01/21/2004)

Country	2000	2030
South America		
Argentina	1426152	2457044
Bolivia	206824	554527
Brazil	4553003	11305516
Chile	494932	1047405
Colombia	883401	2410362
Paraguay	102237	324326
Peru	754087	1960957
Central America		
Cuba	479612	875643
Jamaica	80631	197573
Mexico	2178507	6130209
Panama	59220	153308
Trinidad	60259	124780
North America		
Canada	2006107	3542974
USA	17701942	30312264
World	176525312	370023002

to the elaboration of a list of natural products, evaluated specifically for hypoglycemic effect, of several plants and plant-derived compounds, used as anti-diabetic remedies from South, Central and North America (Tables 2-4). It should be noted that most of the references cited are not first hand observations, but compilations copied from other sources. The original references should be consulted for details on the models or mechanism based bioassays used for testing plant extracts and pure compounds for hypoglycemic activity.

Plants and plant-derived compounds with hypoglicemic activity

In the Americas many plants are used popularly to control diabetes mellitus. This has caused an increase in the number of experimental and clinical investigations directed toward the validation of the anti-diabetic properties, which have been empirically attributed to these remedies.

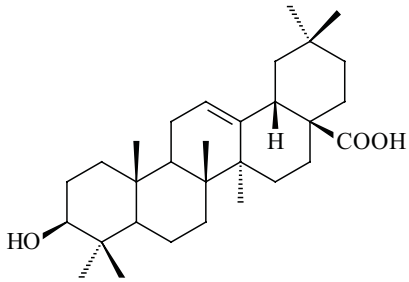
In Brazil, around 200 plants are used empirically to control diabetes mellitus. Of these, fifty two have been experimentally studied and hypoglycaemic activity detected in most of them (See Table 2). *Bauhinia forficata* known popularly as "pata-de-vaca" (cows hoof) is the most studied species. Some studies confirm the activity and others do not. This controversy may be related to the model employed in the experiments. More recently, Pepato et al. (2002) analysed the effects of a leaf decoction as a driking-water substitute for about 1 month on streptozotocin-diabetes (STZ-diabetes) in male Wistar rats. The STZ-diabetic rats treated with the decoction showed a significant reduction in serum and urinary glucose as compared with the STZ-diabetic control, no difference being seen between decoction-treated and -untreated non-diabetic rats.

In Venezuela, the aqueous extract of *B. megalandra* has been used for diabetes mellitus. It was shown to inhibit intestinal glucose absorption in a concentration-dependent way and additive to phlorizine (Gonzalez-Mujica et al., 2003). In addition, the Chilean species *B. candicans* also used for diabetes, presented a significant decrease of glycaemia in alloxan diabetic rats (Lemus et al., 1999).

Phyllanthus sellowianus is a plant used in folk medicine in Argentina as a hypoglycemic and diuretic agent. The aqueous and butanolic extract of this plant, administered at a dose of 200 mg/kg p.o., caused a significant reduction in blood glucose concentration after 6 and 9 h in mice, similar to that observed with glibenclamide (10 mg/kg) which was used as a reference, while the dichloromethane extract of the same plant was ineffective (Hnatyszyn et al., 2002).

Aproximately 150 plants are used in traditional folk medicine in the treatment of diabetes in Mexico (Alarcon-Aguilar et al., 1998). However, only a small number of them have been studied scientifically. The plants most extensively studied are "nopal" *Opuntia streptacantha*, "tronadora" *Tecoma stans,* "Guarumbo" *Cecropia obtusifolia* and "Matarique" *Psacalium decompositum*, (see Table 3). The aqueous extract of the latter species significantly reduced blood glucose in a dose-dependent manner in normal mice after intraperitoneal administration ($P < 0.05$) (Alarcon-Aguilar et al., 2000).

A menu which includes common culinary herbs and spices with hypoglycemic activity for the control



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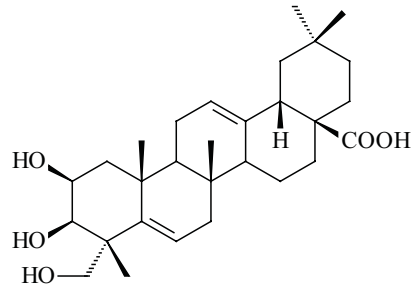

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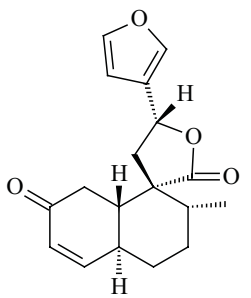

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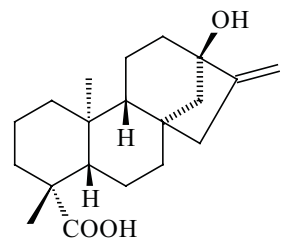

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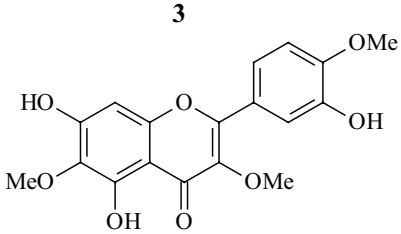

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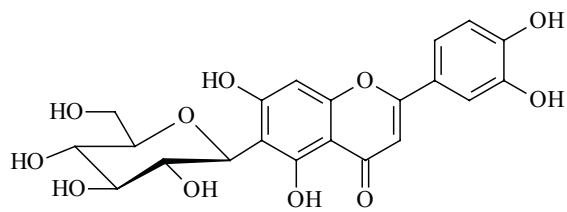

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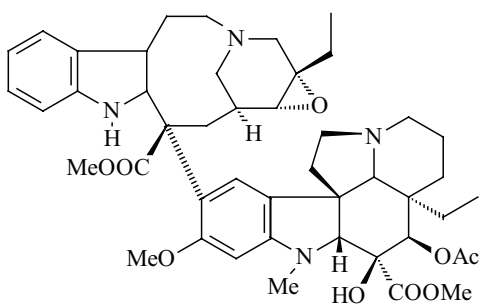

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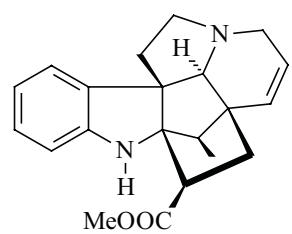

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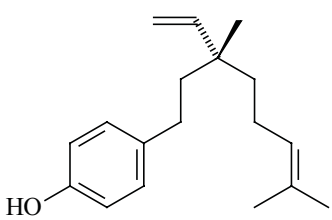

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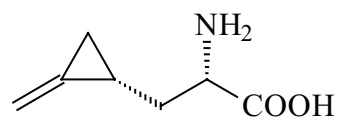

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Figure 1. Representative examples of compounds with hypoglycemic activity.

and prevention of diabetes mellitus was utilized by Broadhurst et al. (2000). To evaluate the possible effects on insulin function, 49 herb, spice, and medicinal plant extracts were tested in the insulin-dependent utilization of glucose using the rat epididymal adipocyte assay. "Cinnamon" *Cinnamomum cassia* was the most bioactive product followed by witch hazel *Hamamelis virginiana*, green and black teas *Camellia sinensis*, allspice *Pimenta officinalis*, bay leaves *Laurus nobilis*, nutmeg *Myristica fragans*, and cloves *Syzigium aromaticum* (see Table 4).

A survey of the literature has shown that a large variety of compounds obtained from several plants of South, Central and North America were found to possess hypoglycemic action. For instance, the triterpenes oleanolic acid (**1**) and bassic acid (**2**) from *Bouvardia terniflora* (Perez et al., 1998) and *Bumelia sartorum* (Naik et al., 1991) respectively lowered blood sugar in test animals. Similarly the diterpenes *trans*-dehydrocrotonin (**3**) from *Croton cajucara* (Farias et al., 1997) and steviol (**4**) from *Stevia rebaudiana* (Ishii; Bracht, 1985) exhibited similar activity. Certain flavonoids ***eg***. 5,7,3-trihydroxy-3,6-4'-trimethoxyflavone (**5**) from *Brickellia veronicaefolia* (Perez et al., 2000a) and the glycoside isoorientin (**6**) from *Cecropia obtusifolia* (Andrade-Cetto et al., 2001) also showed hypoglycaemic effects. A number of alkaloids isolated from *Vinca rosea* (*Catharanthus rosea*) with antitumor activity (Svoboda et al., 1964) were submitted for assay for hypoglycemic effects. The results indicated that catharantine, leurosine (**7**), lochnerine, tetrahydroalstonine, vindoline and vindolinine (**8**) produce varying degrees of blood-sugar reduction. For *Otholobium pubescens* this property was attributed to a phenolic compound bakuchiol (**9**). The amino acid hypoglycine A (**10**) isolated from *Blighia sapida* was particularly effective against diabetes (Kean, 1975; Mills et al., 1987) (Figure 1). The great variety of chemical classes indicate that a variety of mechanisms of action are involved in reduction of the glucose level in blood.

The information recorded in Tables 2-4, has been assembled by continent (South, Central and North America), with the name of the country, plant in alphabetical order, scientific name, family, part used, organism tested, activity and reference. This study has enumerated 224 plants and 40 compounds for which hypoglycemic activity has been reported, as a result of pharmacological studies carried out in various research centers in Argentina, Brazil, Canada, Chile Colombia, Cuba, Jamaica, Mexico, Panama, Paraguay, Peru, Puerto Rico Trinidad and the USA. The ten principal families in which such activity has been reported are Fabaceae (25), Asteraceae (25), Myrtaceae (11), Labiatae (10), Cucurbitaceae (8), Solanaceae (7), Anacardiaceae (6), Euphorbiaceae (6), Rubiaceae (6), and Liliaceae (5).

CONCLUSION

This literature review adds more data to that previously published, since there are many plants in South, Central and North America, which present hypoglycemic effects.

The number of plants described in the literature as having hypoglycemic activity is more or less the same in the three continents. Among the 224 plants studied 73 (33%) are found in South America, 77 (34%) in Central America and 74 (33%) in North America. The countries in each continent with the largest contribution are: Brazil with 52 (23%) of the plants studied, Mexico with 54 (24%) and the USA with 70 (31%). None of the plants with hypoglycemic activity was found in all three continents. The following species stood out for the number of citations reported in the scientific literature in each continent: *Bauhinia forficata* with 8 citations (Brazil), *Opuntia streptacantha* with 5 citations (Mexico) and, *Avena sativa* (USA) with 3 citations.

Of an estimated 250.000 higher plants, less than 1% have been screened pharmacologycally and very few in regard to diabetes mellitus. Therefore, it is prudent to look for options in herbal medicine for diabetes mainly in developing countries because it is a pathological condition associated with high morbidity, mortality and economic impact. None of the plants used in traditional medicine, should be used until safety studies have been completed.

ACKNOWLEDGEMENTS

The authors wish to express their sincere thanks to the College of Pharmacy of the University of Illinois at Chicago, Chicago, Illinois 60612-7231, U.S.A., for helping with the computer aided NAPRALERT and CNPq/FAPESQ-PB/Brazil for financial support.

Table 2. Plant and plant-derived compounds with hypoglycemic activity from South America.

Place and Plant	Family	Part used	Organism tested	Activity	Reference
Argentina					
Bauhinia candicans	Fabaceae	Aqueous extract of the leaves	Dogs	Active	Gallo, 1941
Morus insignis	Moraceae	Aqueous extract of the leaves	Rats	Inactive	Basnet, 1993
		Butanol extract of the leaves	Rats	Active	Basnet, 1993
Phyllanthus sellowianus	Euphorbiaceae	Aqueous extract of the bark	Rats	Active	Gonalons et al., 1926
		Aqueous extract of the stem bark	Rats	Active	Hnatyszyn et al., 1997
		Aqueous and butanol extract of the stem bark	Mice	Active	Hnatyszyn et al., 2002
		Dichloromethane extract of the stem bark	Mice	Inactive	Hnatyszyn et al., 2002
Smallanthus sonchifolius	Asteraceae	Aqueous extract of the leaves	Rats	Active	Aybar et al., 2001
Brazil					
Allium cepa	Liliaceae	Bulb powder	Humans	Active	Oliveira; Saiko, 1989
Anacardium occidentale	Anacardiaceae	Tincture of the bark	Humans	Active	Arduino; Soares 1951; Oliveira; Saito, 1989
		Tincture of the bark	Rats	Active	De Aguiar; Lins, 1958
Annona muricata	Annonaceae	Part used and type of extract not stated	Mice	Active	Neves et al., 2002
Averrhoa carambola	Oxalidaceae	Ethanol extract of the leaves	Rats	Inactive	Provasi et al., 2001
		Aqueous extract of the leaves	Rats	Inactive	Damasceno et al., 2002[a]
Baccharis trimera	Asteraceae	Aqueous extract of the aerial parts	Humans	Active	Oliveira; Saito, 1989
Bauhinia forficata	Fabaceae	Aqueous extract of the leaves	Humans	Active	Juliant, 1931 Oliveira; Saito, 1989
		Aqueous extract of the leaves	Humans	Inactive	Russo et al., 1990
		Aqueous extract of the leaves	Rats	Active	Pepato et al., 2002
		Ethanol extract of the leaves	Rats	Inactive	Almeida; Agra, 1986
		Aqueous extract of the leaves	Rats	Inactive	Volpato et al., 1999
		Butanol extract of the leaves	Rats	Inactive	Silva et al., 2002
		Kaempferol-3,7-*O*-dirhamnoside	Rats	Active	Sousa et al., 2002a

Bauhinia ungulata	Fabaceae	Aqueous extract of the leaves	Rats	Active	Vale et al., 2001
Bidens pilosa	Asteraceae	Aqueous and methanol extract of the aerial parts	*In vitro* α-glucosidase	Inactive	Carvalho et a., 2002
Bowdichia virgilioides	Fabaceae	Aqueous extract of the bark	Humans	Active	Oliveira; Saito, 1989
Brosimum acutifolium	Moraceae	Ethanol extract of the bark	Rats	Inactive	Manrique et al., 2002
Bumelia sartorum	Sapotaceae	Ethanol extract of the stem bark	Rats	Active	Almeida et al., 1985
		Bassic acid	Rats	Active	Naik et al., 1990
Caesalpinea ferrea	Fabaceae	Ethanol extract of the stems	Rats	Inactive	Almeida; Agra, 1986
		Aqueous extract of the bark	Humans	Active	Oliveira; Saito, 1989
Canavalia ensiformis	Fabaceae	Canatoxin	Rats	Active	Ribeiro da Silva et al., 1986 Ribeiro-da-Silva et al., 1990 Ribeiro-da-Silva; Prado, 1993
		Protein	Mice	Active	Oliveira et al., 1999
Chrysobalanus icaco	Chrysobalanaceae	Aqueous extract of the leaves	Mice	Active	Presta; Pereira, 1987
Citrullus vulgaris	Cucurbitaceae	Pulp of the fruits	Humans	Active	Araújo, 1999
Cissus sicyoides	Vitaceae	Leaves - Type of extract not stated	Rats	Active	Mori, 2001
		Aqueous extract of the leaves	Rats	Active	Beltrame et al., 2001 Pepato et al., 2003
Cissus verticillata	Vitaceae	Aqueous extract of the leaves	Rats	Active	Barbosa et al., 2002
Citrus spp	Rutaceae	Soluber fiber pectin	Rats	Active	Derivi et al., 1987
Coffea arabica	Rubiaceae	Seed powder	Mice	Active	Sampaio, 1979
		β-Sitosterol	Mice	Active	Sampaio, 1979
Croton cajucara	Euphorbiaceae	Part used and type of extract not stated	Rats	Active	Cardoso et al., 2002
		Trans-dehydrocrotonin	Rats	Active	Farias et al., 1997
Cymbopogon citratus	Poaceae	Aqueous extract of the leaves	Rats	Inactive	Souza et al., 1986
Dalbergia subynosa	Fabaceae	Part used and type of extract not stated	Guinea pigs	Active	Cardoso et al., 2002
Echinodorus macrophyllys	Alismataceae	Ethanol extract of the leaves	Rats	Active	Camargo et al., 2002
Epidendrum nonsenii	Orchidaceae	Aqueous extract	Rats	Active	Novaes et al., 2001
Eugenia jambolana	Myrtaceae	Ethanol extract of the seeds	Humans	Active	Oliveira; Saito, 1989
		Aqueous extract of the leaves	Rats	Inactive	Pepato et al., 2001
		Aqueous extract of the leaves	Rats	Inactive	Damasceno et al., 2002a
		Sapogenin	Rats	Inactive	Damasceno et al., 2002b
Glechoma hederaceae	Labiatae	Ethanol extract of the leaves	Humans	Active	Oliveira; Saito, 1989
Gymnema sylvestre	Asclepiadaceae	Leaves powder	Rats	Inactive	Galletto et al., 2003

Licania rigida	Chrysobalanaceae	Aqueous extract of the leaves and stems	Rats	Inactive	Almeida; Agra, 1986
Mangifera indica	Anacardiaceae	Aqueous extract of the leaves	Rats	Inactive	Teixeira et al., 1998
		Aqueous extract of the leaves	Humans	Inactive	Teixeira et al., 1998
Marrubium vulgare	Labiatae	Aqueous extract	Rats	Active	Novaes et al., 2001
Myrcia sphaerocarpa	Myrtaceae	Aqueous extract of the leaves	Humans	Active	Oliveira; Saito, 1989
Myrcia uniflora	Myrtaceae	Aqueous extract of the leaves	Humans	Inactive	Russo et al., 1990
		Aqueous extract of the leaves	Rats	Active	Pepato et al., 1993
Nastutium officinale	Cruciferae	Aqueous extract of the entire plant	Humans	Active	Oliveira; Saito, 1989
Periandra mediterranea	Fabaceae	Ethanol extract of the roots	Humans	Active	Oliveira; Saito, 1989
Phrygilanthus acutifolius	Loranthaceae	Aqueous extract of the leaves and stems	Rats	Active	Gomez et al., 2000
Phyllanthus niruri	Euphorbiaceae	Ethanol extract of the aerial parts	Humans	Active	Oliveira; Saito, 1989
Polymnia sonchifolia	Asteraceae	Ethanol extract of the leaves	Mice	Active	Longhi et al., 2003
Punica granatum	Punicaceae	Ethanol extract of the fruits	Mice	Active	Pereira, 1997
Rheedia gardneriana	Cyperaceae	Aqueous extract	Rats	Inactive	Novaes et al., 2001
Ricinus communis	Euphorbiaceae	Aqueous extract of the leaves	Humans	Active	Oliveira; Saito, 1989
Rubus imperialis	Rosaceae	Aqueous extract	Rats	Active	Novaes et al., 2001
		Methanol extract of the roots	Rats	Active	Kanegusuku et al., 2002
Rudgea viburnioides	Rubiaceae	Ethanol extract of the leaves	Rats	Inactive	Silveira et al., 2001
Salvia officinalis	Labiatae	Aqueous extract of the leaves	Humans	Active	Oliveira; Saito, 1989
Solanum lycocarpum	Solanaceae	Starch from the unripe fruits powder	Mice	Inactive	Oliveira et al., 2003
Stevia rebaudiana	Asteraceae	Aqueous extract of the aerial parts	Human	Active	Alvares et al., 1981 Oliveira; Saito, 1989
		Aqueous extract of the leaves	Rats	Inactive	Von Schmeling, 1977
		Steviol and isoesteviol	Rats	Active	Ishii; Bracht, 1985
Syzygium cumini	Myrtaceae	Aqueous extract of the bark	Rats	Inactive	Miron et al., 2002
		Aqueous extract of the leaves	Humans	Inactive	Teixeira et al., 2000
Syzygium jambos	Myrtaceae	Aqueous extract of the leaves	Humans	Inactive	Teixeira, 1990
Syzygium malaccense	Myrtaceae	Part used and type of extract not stated	Mice	Active	Neves et al., 2002
Talauma ovata	Magnoliaceae	Ethanol extract of the leaves	Rats	Inactive	Morato, 1989
Vatairea macrocarpa	Fabaceae	Aqueous extract of the bark	Rats	Inactive	Reis et al., 2002
Vitex megapotamica	Verbenaceae	Ethanol extract of the leaves	Rats	Active	Sousa et al., 2002b
Wedelia paludosa	Asteraceae	Aqueous extract	Rats	Active	Novaes et al., 2001

Chile					
Bauhinia candicans	Fabaceae	Aqueous extract of the leaves	Rats	Active	Lemus et al., 1999
Galega officinalis	Fabaceae	Aqueous extract of the leaves	Rats	Active	Lemus et al., 1999
Geranium core-core	Geraniaceae	Ethanol extract of the whole plant	Rat	Active	Rodriguez et al., 1994
Lupinuse hilli	Fabaceae	Part used and type of extract not stated	Humans	Equivocal	Diaz et al., 1990
Morus alba	Moraceae	Aqueous extract of the leaves	Rats	Active	Lemus et al., 1999
Oxalis rosea	Oxalidaceae	Ethanol extract of the whole plant	Rats	Inactive	Rodriguez et al., 1994
Plantago major	Plantaginaceae	Ethanol extract of the whole plant	Rats	Inactive	Rodriguez et al., 1994
Rubus ulmifolius	Rosaceae	Aqueous extract of the leaves	Rats	Active	Lemus et al., 1999
Colombia					
Curatella americana	Anacardiaceae	Chloroform extract of the bark	Rats	Active	Ospina et al., 1995
Paraguay					
Eugenia uniflora	Myrtaceae	Aqueous extract of the leaves	Mice	Active	Matsumura et al., 2000
		Aqueous extract of the leaves	Monkeys	Inactive	Ferro et al., 1988
Hexachlamys edulis	Myrtaceae	Ethanol extract of the leaves and stems	Rats	Active	Rodriguez et al., 1992
Stevia rebaudiana	Asteraceae	Aqueous extract of the leaves	Humans	Active	Oviedo et al., 1970
Peru					
Aloe vera	Liliaceae	Juice of the leaves	Rats	Active	Valencia et al., 1994
Cyclanthera pedata	Cucurbitaceae	Aqueous extract of the leaves	Rats	Active	Valencia et al., 1994
Gentianella thyrsoides	Gentianaceae	Aqueous extract of the roots and stems	Rats	Active	Tomas et al., 1999
		Dichloromethane extract of the roots and stems	Rats	Active	Tomas et al., 1999
		Methanol extract of the roots and stems	Rats	Equivocal	Tomas et al., 1999
Otholobium pubescens	Fabaceae	Bakuchiol	Rats	Active	Krenisky et al., 1999
Venezuela					
Bauhinia megalandra	Fabaceae	Aqueous extract of the leaves	Rats	Active	Gonzalez-Mujica et al., 2003

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Table 3. Plant and plant-derived compounds with hypoglycemic activity from Central America.

Place and Plant	Family	Part used	Organism tested	Activity	Reference
Cuba					
Bidens alba	Asteraceae	Ethanol extract of the leaves	Rats	Inactive	Guerra, 2001
Bougainvillea spectabilis	Nyctaginaceae	Ethanol extract of the leaves	Rats	Inactive	Salvado et al., 1997
Ocimum sanctum	Labiatae	Ethanol extract of the leaves	Rats	Active	Deas-Rodriguez et al., 1988; 1997
Petiveria alliaceae	Phytolacaceae	Ethanol extract of the leaves	Mice	Active	Lores et al., 1990
		Ethanol extract of the roots	Mice	Inactive	Lores et al., 1990
		Ethanol extract of the stems	Mice	Active	Lores et al., 1990
		Aqueous extract of the leaves	Humans	Inactive	Rojo-Domínguez et al., 2002
Phyllanthus embira	Euphorbiaceae	Aqueous ext. of the leaves	Mice	Active	Cuellar; Estevez, 1980
		Fagasterol	Mice	Active	Cuellar; Estevez, 1980
Jamaica					
Anacardium occidentale	Anacardiaceae	Aqueous extract of the bark	Dogs	Week activity	Morrison et al., 1982
Bixa orellana	Bixaceae	Chloroform extract of the seeds	Dogs	Active	Morrison et al., 1985
		Aqueous ext. of the seeds	Dogs	Active	Morrison et al., 1982
Blighia sapida	Sapindaceae	Arrilus powder	Humans	Active	Kean, 1975
		Fruits powder	Humans	Active	Jelliffe; Stuart, 1954 Bressler, 1976
		Hypoglycine A	Rats	Active	Kean, 1975 Mills et al., 1987
Cannabis sativa	Canabaceae	Aqueous extract of the resine	Dogs	Weak activity	Morrison et al., 1982
Capsicum frutescens	Solanaceae	Aqueous extract of the seeds	Dogs	Active	Morrison et al., 1982
Cassia alata	Fabaceae	Aqueous extract of the leaves	Dogs	Active	Morrison et al., 1982
Catharanthus roseus	Apocynaceae	Aqueous extract of the leaves	Dogs	Active	Morrison et al., 1982
Cocos nucifera	Arecaceae	Aqueous extract of the shell	Dogs	Weak activity	Morrison et al., 1982
Colocasia esculenta	Araceae	Ethanol extract of the tuber	Rats	Active	Grindley et al., 2002
Dioscorea cayenensis	Dioscoreaceae	Ethanol extract of the tuber	Rats	Weak activity	Grindley et al., 2002
Mikania micrantha	Asteraceae	Aqueous extract of the aerial parts	Dogs	Weak activity	Morrison et al., 1982
Momordica charantia	Cucurbitaceae	Aqueous extract of the fruits	Dogs	Weak activity	Morrison et al., 1982
Spondias dulcis	Anacardiaceae	Aqueous extract of the fruits	Dogs	Weak activity	Morrison et al., 1982
Symphytum officinale	Boraginaceae	Aqueous extract of the leaves	Dogs	Weak activity	Morrison et al., 1982
Mexico					
Acourtia thurberi	Asteraceae	Aqueous extract of the roots	Rats and rabbits	Active	Alarcon-Aguilar et al., 1997
Acrocomia mexicana	Palmae	Aqueous extract of the roots	Rats	Active	Perez et al., 1984
		Coyolose	Mice	Active	Perez et al., 1997
Agarista mexicana	Ericaceae	Chloroform extract of the bark	Mice and rats	Active	Perez et al., 1996
Aloe vera	Liliaceae	Juice of the stems	Rabbits	Active	Roman-Ramon et al., 1991

Arachis hypogaea	Fabaceae	Seeds powder	Humans	Inactive	Frati-Munari et al., 1991
Argemone mexicana	Papaveraceae	Aqueous extract of the flowers	Dogs	Inactive	Meckes-Lozoya et al., 1986
Bidens leucantha	Asteraceae	Aqueous extractof entire plant	Mice	Active	Perez et al., 1984
Bidens pilosa	Asteraceae	Aqueous extract of entire plant	Mice	Active	Perez et al., 1984
Bouvardia terniflora	Rubiaceae	Chloroform extract of the stems	Mice	Active	Perez et al., 1998a
		Oleanolic acid	Mice	Active	Perez et al., 1998a
		Ursolic acid	Mice	Active	Perez et al., 1998a
Brickellia veronicaefolia	Asteraceae	5,7,3´-trihydroxy-3,6,4´-trimethoxyflavone	Mice	Active	Perez et al., 2000a
Cacalia decomposita	Asteraceae	Aqueous extract of the roots	Mice	Active	Perez et al., 1984
Calamintha macrostema	Labiatae	Aqueous extract of the roots	Mice	Active	Perez et al., 1984
Capraria biflora	Srophulariaceae	Aqueous extract of the leaves	Mice	Active	Perez et al., 1984
Cecropia obtusifolia	Cecropiaceae	Aqueous extract of the leaves	Mice	Active	Mellado et al., 1984
		Aqueous extract of the leaves	Rabbits	Weak actitity	Roman-Ramos et al., 1991
		Aqueous extract of the leaves	Mice	Active	Perez et al., 1984
		Aqueous and butanol extract of the leaves	Rats	Active	Andrade-Cet; Wiedenfel, 2001
		Chlorogenic acid	Rats	Active	Andrade-Cet; Wiedenfel, 2001
		Isoorientin	Rats	Active	Andrade-Cet; Wiedenfel, 2001
Cirsium pascuarense	Asteraceae	Hexane extract of the leaves	Mice	Active	Perez et al., 2001
		Chloroform and methanol extract of the leaves	Mice	Inactive	Perez et al., 2001
Coutarea latiflora	Rubiaceae	Part used and type of extract not stated	Rabbits	Inactive	Guerra, 1947
		Aqueous ext. of the leaves	Mice	Active	Perez et al., 1984
Cucurbita ficifolia	Cucurbitaceae	Juice of the fruits	Rabbits	Active	Roman-Ramos et al., 1991
		Juice of the fruits	Mice	Active	Alarcon-Aguilar et al., 2002a
		Juice of the fruits	Humans	Active	Acosta-Patino et al., 2001
Equisetum myriochaetum	Equisetaceae	Aqueous extract of the aerial parts	Humans	Active	Revilla et al., 2002
		Aqueous and butanol extract of the aerial parts	Rats	Active	Andrade-Cetto et al., 2000
		Kaempferol-3-O-sophoroside-4'-O-β-D-glucoside	Rats	Active	Andrade-Cetto et al., 2000
Eriobotrya japonica	Rosaceae	Aqueous extract of the leaves	Rabbits	Weak activity	Roman-Ramos et al., 1991
Eucalyptus globulus	Myrtaceae	Aqueous extract of the leaves	Mice	Active	Perez et al., 1984
Euphorbia prostata	Euphorbiaceae	Aqueous extract of the entire plant	Rabbits	Active	Alarcon-Aguilar et al., 1998

Eysenhardtia polystachya	Lotoidaceae	Aqueous extract of the entire plant	Mice	Activa	Perez et al., 1984
Gnaphalium semiamplexicaule	Asteraceae	Aqueous extract of the flowers	Dogs	Weak activity	Meckes-Lozoya et al., 1986
Guazuma ulmifolia	Sterculiaceae	Aqueous extract of the leaves	Rabbits	Active	Alarcon-Aguilar et al., 1998
Ibervillea sonorae	Cucurbitaceae	Aqueous extract of the roots	Mice and rats	Active	Alarcon-Aguilar et al., 2002b
Lepechinia caulescens	Lamiaceae	Aqueous and methanol extract of the aerial parts	Mice	Active	Roman-Ramos et al., 1991
		Hexane, methylene chloride, methanol and aqueous ext of the flowers	Mice	Inactive	Roman-Ramos et al., 2001
		Aqueous ext of the leaves	Rabbits	Active	Alarcon-Aguilar et al., 1998
Loeselia mexicana	Polemoniaceae	Aqueous extract of the entire plant	Mice	Active	Perez et al., 1984
Musa sapientum	Musaceae	Aqueous ext of the leaves	Rabbits	Active	Alarcon-Aguilara et al., 1998
Opuntia ficus-indica	Cactaceae	Leaves powder	Humans	Active	Frati-Munari et al., 1991
Opuntia sp	Cactaceae	Stem powder	Humans	Inactive	Frati-Munari et al., 1987
Opuntia streptacantha	Cactaceae	Aqueous extract of the aerial parts	Humans	Active	Frati-Munari et al., 1989
		Stem powder	Humans	Inactive	Frati-Munari et al., 1990
		Juice of the stems	Rabbits	Active	Roman-Ramos et al., 1991
		Sap powder of the stems	Dogs	Active	Ibanez-Camacho et al., 1983
		Leaves powder	Rats	Active	Ibanez-Camacho et al., 1979
Oryza sativa	Poaceae	Seed powder	Humans	Inactive	Frati-Munari et al., 1991
Parmantiera edulis	Bignoniaceae	Aqueous ext. of the roots	Mice	Inactive	Perez et al., 1984
		Lactucin-8-*O*-methylacrylate	Rats	Active	Perez et al., 2000b
Phaseolus vulgaris	Fabaceae	Aqueous extract of the pods	Rabbits	Weak activity	Roman-Ramos et al., 1991
Plantago psyllium	Plantaginaceae	Mucilage	Humans	Active	Frati-Munari et al., 1985
Psacalium decompositum	Asteraceae	Chromatographic fraction of the roots	Mice	Active	Alarcon-Aguilar et al., 2000
		Aqueous extract of the roots	Rats and rabbits	Active	Alarcon-Aguilar et al., 1997
		Aqueous extract of the roots	Mice	Active	Alarcon-Aguilar et al., 2000
		Hexane extract of the roots	Mice	Inactive	Alarcon-Aguilar et al., 2000
		Cacalol, cacalone and maturin	Mice	Inactive	Alarcon-Aguilar et al., 2000
Psacalium peltatum	Asteraceae	Aqueous ext. of the roots	Rats and rabbits	Active	Alarcon-Aguilar et al., 1997
		Aqueous ext. of the roots	Rabbits	Active	Roman-Ramos et al., 1991
Psittacanthus calyculatus	Loranthaceae	Aqueous extract of the flowers	Mice	Active	Perez et al., 1984
Rhizophora mangle	Rizophoraceae	Aqueous extract of the leaves	Rabbits	Active	Alarcon-Aguilar et al., 1998
Salpianthus arenarius	Nyctaginaceae	Aqueous extract of the flowers	Mice	Active	Perez et al., 1984

Salpianthus macrodontus	Nyctaginaceae	Leaves and stems - Type of extract not stated	Rabbits	Weak activity	Roman-Ramos et al., 1991
Sambucus mexicana	Caprifoliaceae	Aqueous extract of the flowers	Dogs	Inactive	Meckes-Lozoya et al., 1986
Solanum tuberosum	Solanaceae	Tuber powder	Humans	Inactive	Frati-Munari et al., 1991
Solanumm verbascifolium	Solanaceae	Aqueous extract of the leaves and stems	Rabbits	Active	Roman-Ramos et al., 1991
Tecoma stans	Bignoniaceae	Aqueous extract of the leaves and stems	Rabbits	Weak activity	Roman-Ramos et al., 1991
		Aqueous extract of the leaves	Rats	Active	Aguilar et al., 1993
		Part used and type of extract not stated	Rabbits	Inactive	Guerra, 1946
		Aqueous extract of the entire plant	Mice	Active	Perez et al., 1984
Teucrium cubense	Lamiaceae	Aqueous extract of the leaves and stems	Rabbits	Weak activity	Roman-Ramos et al., 1991
Tournefortia hirsutissima	Boraginaceae	Aqueous extract of the leaves	Rabbits	Active	Alarcon-Aguilar et al., 1998
Trigonella foenum-graceum	Fabaceae	Aqueous extract of the leaves	Rabbits	Active	Alarcon-Aguilar et al., 1998
Turnera diffusa	Turneraceae	Aqueous extract of the leaves	Mice	Active	Perez et al., 1984
		Aqueous extract of the leaves	Rabbits	Active	Alarcon-Aguilar et al., 1998
Valeriana officinalis	Valerianaceae	Aqueous extract of the roots	Mice	Active	Perez et al., 1984
Valeriana edulis ssp. procera	Valerianaceae	Aqueous extract of the roots	Mice	Active	Perez et al., 1984
Verbesina crocata	Asteraceae	Aqueous extract of the flowers	Mice	Active	Perez et al., 1984
Verbesina persicifolia	Asteraceae	Aqueous extract of the leaves	Mice	Active	Perez et al., 1984
		Chloroform extract of the bark	Mice and rats	Active	Perez et al., 1996
Zea mays	Poaceae	Seed powder	Humans	Inactive	Frati-Munari et al., 1991
Panama					
Cajanus cajan	Fabaceae	Aqueous extract of the leaves	Rats	Active	Avellar et al., 1991
Cassia fistula	Fabaceae	Aqueous extract of the leaves	Rats	Active	Avellar et al., 1991
Neurolaena lobata	Asteraceae	Ethanol extract of the leaves	Mice	Active	Gupta et al., 1984
Momordica charantia	Cucurbitaceae	Aqueous extract of the vine	Rabbits	Active	Rivera, 1942
		Alkaloid fraction	Rabbits	Inactive	Rivera, 1942
Trinidad					
Momordica charantia	Cucurbitaceae	Aqueous extract of the leaves, flowers and stems	Mice	Active	Bailey et al., 1985

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Table 4. Plant and plant-derived compounds with hypoglycemic activity from North America.

Place and Plant	Family	Part used	Organism tested	Activity	Reference
Canada					
Avena sativa	Poaceae	Gum powder	Humans	Active	Braaten et al., 1991
Fatsia horrida	Araliaceae	Aqueous extract of the rootbark	Rabbits	Active	Large et al., 1938
Panax quinquefolius	Araliaceae	Saponin fraction of the roots	Rats	Weak activity	Martinez et al., 1984
		Aqueous extract of the roots	Humans	Active	Vuksan et al., 2000
		Ginsenoside	Humans	Inactive	Sievenpiper et al., 2003
Rhus typhina	Anacardiaceae	Aqueous extract	Rats and dogs	Active	Fortier, 1949
USA					
Abutilon theophrasti	Malvaceae	Seeds powder in ration	Rats	Active	Dugan et al., 1990a
Allium sativum	Liliaceae	Bulb powder in ration	Rats	Inactive	Chi et al., 1982
		Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
Aloe vera	Liliaceae	Leaves powder	Rats	Inactive	Herlihy et al., 1998
Anethum graveolens	Umbelliferae	Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
Apium graveolens	Umbelliferae	Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
Arachis hypogaea	Fabaceae	Part used and type of extract not stated	*In vitro* cells	Week activity	Broadhurst et al., 2000
Astragalus membranaceus	Fabaceae	Part used and type of extract not stated	*In vitro* cells	Week activity	Broadhurst et al., 2000
Atriplex halimus	Chenopodiaceae	Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
Avena sativa	Poaceae	Brun powder	Pigs	Active	Knudsen et al., 1995
		Brun powder	Humans	Active	Hopewell et al., 1993
		Part used and type of extract not stated	*In vitro* cells	Weak activity	Broadhurst et al., 2000
Brassica nigra	Cruciferae	Part used and type of extract not stated	*In vitro cells*	Inactive	Broadhurst et al., 2000
Brassica oleraceae	Brassicaceae	Ethanol extract of the aerial parts	*Rats*	Active	Dubin et al., 1928
Camellia sinensis	Theaceae	Part used and type of extract not stated	*In vitro cells*	Active	Broadhurst et al., 2000
Cannabis sativa	Cannabaceae	Leaves - Smoking	*Humans*	Inactive	Podolsky et al., 1971
Capsicum annum	Solanaceae	Part used and type of extract not stated	*In vitro cells*	Inactive	Broadhurst et al., 2000

Carica papaya	Caricaceae	Fruits powder	Rabbits	Inactive	Bischoff et al., 1929
Carya illinoensis	Juglandaceae	Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
Chimaphila umbellata	Pyrolaceae	Buthanol extract of the leaves	Rats	Inactive	Williams et al., 1959
		Cystine	Rats	Inactive	Williams et al., 1959
		Indole-3-acetic acid	Rats	Inactive	Williams et al., 1959
Cinchona sp.	Rubiaceae	Quinine	Humans	Inactive	Taylor et al., 1988
Cinnamomum cassia	Lauraceae	Part used and type of extract not stated	*In vitro* cells	Active	Broadhurst et al., 2000
Cinnamomum verum	Lauraceae	Part used and type of extract not stated	*In vitro* cells	Active	Broadhurst et al., 2000
Coffea arabica	Rubiaceae	Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
		Caffeine	Humans	Active	Kerr et al., 1993
Curcuma longa	Zingiberaceae	Part used and type of extract not stated	*In vitro* cells	Week activity	Broadhurst et al., 2000
Echinaceae purpurea	Asteraceae	Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
Elettaria cardamomum	Zingiberaceae	Part used and type of extract not stated	*In vitro cells*	Inactive	Broadhurst et al., 2000
Eleutherococcus senticosus	Araliaceae	Part used and type of extract not stated	*In vitro cells*	Inactive	Broadhurst et al., 2000
Eupatorium urticaefolium	Asteraceae	Fluid extact of the aerial parts	*Dogs*	Inactive	Cartland et al., 1931
Fatsia horrida	Araliaceae	Aqueous extract of the bark	*Humans*	Active	Smith, 1983
		Aqueous extract	*Rats*	Inactive	Williams et al., 1959
Ginkgo biloba	Ginkgoaceae	Aqueous extract	*Humans*	Active	Kudolo, 2001
Grifola frondosa	Basidiomycete	Polysaccharide caplets	*Humans*	Active	Konno et al., 2002
Glycine max	Fabaceae	Part used and type of extract not stated	*In vitro cells*	Week activity	Broadhurst et al., 2000
Gossypium herbaceum	Malvaceae	Pulp powder of the seeds	*Ewes*	Active	Menaul, 1923
Gymnema sylvestre	Asclepiadaceae	Part used and type of extract not stated	*In vitro cells*	Inactive	Broadhurst et al., 2000
Hamamelis virginiana	Hamamelidaceae	Part used and type of extract not stated	*In vitro cells*	Active	Broadhurst et al., 2000

Humulus lupulus	Cannabaceae	Colupulone	Mice	Active	Mannering et al., 1994
Ipomoea hederaceae	Convolvulaceae	Seeds powder	Rats	Active	Dugan et al., 1990
Ipomoea lacunosa	Convolvulaceae	Seeds powder	Rats	Active	Dugan et al., 1990
Laurus nobilis	Lauraceae	Part used and type of extract not stated	*In vitro* cells	Active	Broadhurst et al 2000
Linum usitatissimum	Linaceae	Part used and type of extract not stated	*In vitro* cells	Week activity	Broadhurst et al., 2000
Lupinus sp	Fabaceae	Aqueous extract of the seeds	Humans	Inactive	Tsiodras et al., 1999
Medicago sativa	Fabaceae	Aqueous extract of the entire plant	Rats	Inactive	Williams et al., 1959
Momordica charantia	Cucurbitaceae	Fraction peptide MC-6	Rats	Active	Nag, 2000
		Fraction peptide MC-6.1	Rats	Active	Nag, 2000
		Fraction peptide MC-6.2	Rats	Active	Nag, 2000
		Fraction peptide MC-6.3	Rats	Active	Nag, 2000
Morus indica	Moraceae	Aqueous extract of the leaves	Humans	Active	Andallu et al., 2001
Myristica fragans	Myristicaceae	Part used and type of extract not stated	In vitro cells	Active	Broadhurst et al., 2000
Nepeta cataria	Labiatae	Part used and type of extract not stated	In vitro cells	Inactive	Broadhurst et al., 2000
Ocimum basilicum	Labiatae	Part used and type of extract not stated	In vitro cells	Active	Broadhurst et al., 2000
Ocimum sanctum	Labiatae	Aqueous extr. of the entire plant	Organism not stated	Active	Luthy; Martinez 1964
Origanum vulgare	Labiatae	Part used and type of extract not stated	In vitro cells	Active	Broadhurst et al., 2000
Panax ginseng	Araliaceae	Part used and type of extract not stated	In vitro cells	Week activity	Broadhurst et al., 2000
Panax quinquefolius	Araliaceae	Saponin fraction of the roots	Rats	Weak activity	Martinez et al., 1984
		Part used and type of extract not stated	In vitro cells	Weak activity	Broadhurst et al., 2000
Petroselinum crispum	Umbelliferae	Part used and type of extract not stated	In vitro cells	Inactive	Broadhurst et al., 2000
Pimenta officinalis	Myrtaceae	Part used and type of extract not stated	In vitro cells	Active	Broadhurst et al., 2000
Pimpinella anisum	Umbelliferae	Part used and type of extract not stated	In vitro cells	Inactive	Broadhurst et al., 2000
Piper nigrum	Piperaceae	Part used and type of extract not stated	In vitro cells	Inactive	Broadhurst et al., 2000

Plantago ovata	Plantaginaceae	Seed husks in ration	Mice	Inactive	Watters et al., 1989
Prunus dulcis	Rosaceae	Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
Rosmarinus officinalis	Labiatae	Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
Salvia officinalis	Labiatae	Part used and type of extract not stated	*In vitro* cells	Week activity	Broadhurst et al., 2000
Solanum nigrum	Solanaceae	Seeds powder	Rats	Active	Dugan et al., 1990a
Stevia rebaudiana	Asteraceae	Leaves - Type of extract not stated	Dogs	Inactive	White jr et al., 1994
Syzigium aromaticum	Myrtaceae	Part used and type of extract not stated	*In vitro* cells	Active	Broadhurst et al., 2000
Tecoma stans	Bignoniaceae	Aqueous extract	Mice	Inactive	Nash, 1958
Tillandsia usneoides	Bromeliaceae	Aqueous extract of the entire plant	Mice	Active	Keller et al., 1981
		3-Hydroxy-3-methyl-glutaric acid	Mice	Active	Witherup; McLaughlin, 1995
		Succinic acid	Mice	Inactive	Witherup; McLaughlin, 1995
		4',5,7-Trihydroxy-3,3',5',6-tetramethoxy-7-*O*-β-D-glucoside	Mice	Inactive	Witherup; McLaughlin, 1995
Vaccinium corymbosum	Ericaceae	Ethanol extract of the leaves	Dogs	Inactive	Allen, 1927
Vaccinium myrtillus	Ericaceae	Ethanol ext. of the leaves	Dogs	Inactive	Allen, 1927
Vaccinium pennsylvanicum	Ericaceae	Aqueous extrac of the leaves	Dogs	Inactive	Allen, 1927
Vanilla planifolia	Orchidaceae	Part used and type of extract not stated	*In vitro* cells	Week activity	Broadhurst et al., 2000
Vinca rosea	Apocynaceae	Ajmalicine	Rats	Inactive	Svoboda et al., 1964
		Catharantine	Rats	Questionable	Svoboda et al., 1964
		Leurosine	Rats	Moderated act.	Svoboda et al., 1964
		Lochnerine	Rats	Slight activity	Svoboda et al., 1964
		Perivine	Rats	Inactive	Svoboda et al., 1964
		Sitsirikine	Rats	Inactive	Svoboda et al., 1964
		Tetrahydroalstonine	Rats	Questionable	Svoboda et al., 1964
		Vincathicine	Rats	Inactive	Svoboda et al., 1964
		Vindoline	Rats	Slight activity	Svoboda et al., 1964
		Vindolinine	Rats	Moderated act.	Svoboda et al., 1964
Withania somnifera	Solanaceae	Part used and type of extract not stated	*In vitro* cells	Inactive	Broadhurst et al., 2000
Xanthium strumarium	Asteraceae	Ethanol extract of the entire plant	Rabbits	Active	Turner et al., 1974
Zingiber officinale	Zingiberaceae	Part used and type of extract not stated	*In vitro* cells	Week activity	Broadhurst et al., 2000

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