Revisão

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

José M. Barbosa-Filho*, Tereza H.C. Vasconcelos, Adriana A. Alencar, Leônia M. Batista, Rinalda A.G. Oliveira, Diego N. Guedes, Heloina de S. Falcão, Marcelo D. Moura, Margareth F.F.M. Diniz, João Modesto-Filho

Laboratório de Tecnologia Farmacêutica "Delby Fernandes de Medeiros", Universidade Federal da Paraíba, Caixa Postal 5009, 58051-970, João Pessoa, PB, Brazil

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

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 dosedependent 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

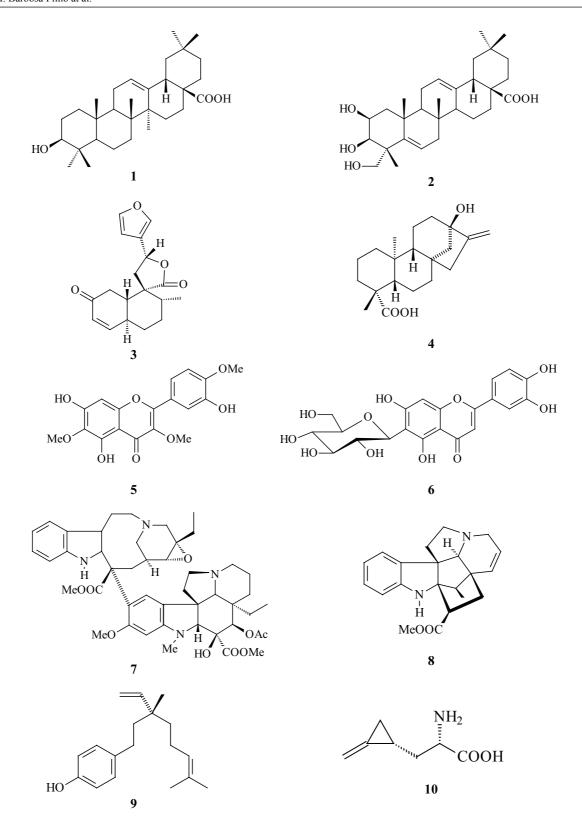


Figure 1. Representative examples of compounds with hypoglycemic activity.

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. 5,7,3trihydroxy-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 Brazil	Asteraceae	Aqueous extract of the leaves	Rats	Active	Aybar et al., 2001
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	Mice	Active	Neves et al., 2002
		not stated			
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	Humans	Active	Oliveira; Saito, 1989
		parts			
Bauhinia forficata	Fabaceae	Aqueous extract of the leaves	Humans	Active	Juliant, 1931
			;	,	Unveira; Sailo, 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-	Rats	Active	Sousa et al., 2002a
		dirhamnoside			

Bauhinia ungulata	Fahaceae	Aqueous extract of the leaves	Rafs	Active	Vale et al., 2001
Bidens pilosa	Asteraceae	Aqueous and methanol extract	In vitro	Inactive	Carvalho et a., 2002
		of the aerial parts	α -glucosidase		
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	Rats	Active	Almeida et al., 1985
		bark			
		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	Rats	Active	Mori, 2001
		Stated			
		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	Rats	Active	Cardoso et al., 2002
		Trans-dehydrocrotonin	Pate	Activo	Familiae at al 1007
	ć	A semipal octorium	nats Dete	Tuesting	Carres et al., 1997
Cymbopogon curatus Dalbovaia eubinoea	гоасеае Езрасезе	Aqueous extract of the leaves	Rats Guipes wice	A crive	Souza et al., 1900 Cardoso et al. 2002
Luivei giu suoynosu	1 agascas	not stated	Guinea pigs	2000	(al to 50 ct 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	Kats	Inactive	Galletto et al., 2003

Almeida; Agra, 1986	Teixeira et al., 1998	1 elxella et al., 1998 Noviges et al. 2001	Olivaine: Coita 1080	Onvend, 5ano, 1969 Russo et al. 1000	Pepato et al., 1993	Oliveira; Saito, 1989		Oliveira; Saito, 1989	Gomez et al., 2000	Oliveira; Saito, 1989		Longhi et al., 2003	Pereira, 1997	Novaes et al., 2001	Oliveira; Saito, 1989	Novaes et al., 2001	Kanegusuku et al., 2002	Silveira et al., 2001	Oliveira; Saito, 1989	Oliveira et al., 2003		Alvares et al., 1981	Oliveira; Saito, 1989	Von Schmeling, 1977	Ishii; Bracht, 1985	Miron et al., 2002	Teixeira et al., 2000	Teixeira, 1990	Neves et al., 2002	Morato, 1989	Reis et al., 2002	Sousa et al., 2002b	Novaes et al., 2001
Inactive	Inactive	Inactive Active	Active	Inactive	Active	Active		Active	Active	Active		Active	Active	Inactive	Active	Active	Active	Inactive	Active	Inactive		Active		Inactive	Active	Inactive	Inactive	Inactive	Active	Inactive	Inactive	Active	Active
Rats	Rats	riumans Pats	nats Umasas	Humans	Rats	Humans		Humans	Rats	Humans		Mice	Mice	Rats	Humans	Rats	Rats	Rats	Humans	Mice		Human		Rats	Rats	Rats	Humans	Humans	Mice	Rats	Rats	Rats	Rats
Aqueous extract of the leaves and stems	Aqueous extract of the leaves	Aqueous extract of the leaves	Adueous extract	Aqueous extract of the leaves	Aqueous extract of the leaves	Aqueous extract of the entire	plant	Ethanol extract of the roots	Aqueous extract of the leaves and stems	Ethanol extract of the aerial	parts	Ethanol extract of the leaves	Ethanol extract of the fruits	Aqueous extract	Aqueous extract of the leaves	Aqueous extract	Methanol extract of the roots	Ethanol extract of the leaves	Aqueous extract of the leaves	Starch from the unripe fruits	powder	Aqueous extract of the aerial	parts	Aqueous extract of the leaves	Steviol and isoesteviol	Aqueous extract of the bark	Aqueous extract of the leaves	Aqueous extract of the leaves	Part used and type of extract not stated	Ethanol extract of the leaves	Aqueous extract of the bark	Ethanol extract of the leaves	Aqueous extract
Chrysobalanaceae	Anacardiaceae	Lobiotoe	Lablatae	Myrtaceae	1v1 y1 taccac	Cruciferae		Fabaceae	Loranthaceae	Euphorbiaceae		Asteraceae	Punicaceae	Cyperaceae	Euphorbiaceae	Rosaceae		Rubiaceae	Labiatae	Solanaceae		Asteraceae				Myrtaceae		Myrtaceae	Myrtaceae	Magnoliaceae	Fabaceae	Verbenaceae	Asteraceae
Licania rigida	Mangifera indica	Mammilian	Marrablam Valgare	Myrcia sphaerocarpa Myrcia miiflora	Myrcia anthora	Nastutium officinale		Periandra mediterranea	Phrygilanthus acutifolius	Phyllanthus niruri		Polymnia sonchifolia	Punica granatum	Rheedia gardneriana	Ricinus communis	Rubus imperialis		Rudgea viburnioides	Salvia officinalis	Solanum lycocarpum		Stevia rebaudiana				Syzygium cumini		Syzygium jambos	Syzygium malaccense	Talauma ovata	Vatairea macrocarpa	Vitex megapotamica	Wedelia paludosa

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	Rat	Active	Rodriguez et al., 1994
Lupinuse hilli	Fabaceae	Part used and type of extract	Humans	Equivocal	Diaz et al., 1990
:		not stated			
Morus alba Ovalis vasaa	Moraceae	Aqueous extract of the leaves Ethanol extract of the whole	Rats Pats	Active Inactive	Lemus et al., 1999 Rodriguez et al., 1994
Caulis Fosed	Ovalluaccac	plant	Nats	Illactive	Nounguez of al., 1994
Plantago major	Plantaginaceae	Ethanol extract of the whole plant	Rats	Inactive	Rodriguez et al., 1994
Rubus ulmifolius Colombia	Rosaceae	Aqueous extract of the leaves	Rats	Active	Lemus et al., 1999
Curatella americana	Anacardiaceae	Chloroform extract of the bark	Rats	Active	Ospina et al., 1995
Paraguav					
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	Rats	Active	Rodriguez et al., 1992
Stevia rebaudiana	Asteraceae	Aqueous extract of the leaves	Humans	Active	Oviedo et al., 1970
Aloewera	T iliaceae	Tinice of the leaves	Rate	Active	Valencia et al 1994
Cyclouthera pedata	Cucurhitaceae	Amenis extract of the leaves	Rats	Active	Valencia et al 1994
Gentianella thyrsoides	Gentianaceae	Aqueous extract of the roots	Rats	Active	Tomas et al., 1999
		and stems			
		Dichloromethane extract of	Rats	Active	Tomas et al., 1999
		the roots and stems			
		Methanol extract of the roots and stems	Rats	Equivocal	Tomas et al., 1999
Otholobium pubescens	Fabaceae	Bakuchiol	Rats	Active	Krenisky et al., 1999
Venezuela Raubinia magalandra	Fa h aceae	Amount extract of the leaves Bate	Rate	Active	Gonzalez-Muiica et al 2003
Danning megalanara	Labaccac	Aducous cattact of tile reaves	Mats	ACIIVO	Conzaicz-iniujica et ai., 2003

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
		A amount out of the goods	Dogs	Activo	Mounison of al 1000
Dlimbia	Consist decore	Aqueous ext. of the seeds	Lugs	Active	Voc. 1075
bugnid sapidd	Sapindaceae	Arrilus powder	numans	Active	Nean, 1973
		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	Agueous extract of the shell	Dogs	Weak activity	Morrison et al., 1982
Colocasia esculenta	Araceae	Ethanol extract of the tuber	Rats	Active	Grindlev et al., 2002
Dioscorea cavenensis	Dioscoreaceae	Ethanol extract of the tuber	Rats	Weak activity	Grindley et al., 2002
Mikania micrantha	Asteraceae	Aqueous extract of the aerial	Dogs	Weak activity	Morrison et al., 1982
		parts	1	•	
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 Mexico	Boraginaceae	Aqueous extract of the leaves	Dogs	Weak activity	Morrison et al., 1982
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	Mice and rats	Active	Perez et al., 1996
	- 11: 1	bark	D-111.		t
Aloe vera	Liliaceae	Juice of the stems	Kabbits	Active	Koman-Kamon 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′-	Mice	Active	Perez et al., 2000a
		trimethoxyflavone			
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	Rats	Active	Andrade-Cet; Wiedenfel, 2001
		the leaves			
		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	Mice	Inactive	Perez et al., 2001
		extract of the leaves			
Coutarea latiflora	Rubiaceae	Part used and type of extract	Rabbits	Inactive	Guerra, 1947
		not stated			
		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	Humans	Active	Revilla et al., 2002
		parts			
		Aqueous and butanol extract of	Rats	Active	Andrade-Cetto et al., 2000
		the aerial parts			
		Kaempferol-3-O-sophoroside-	Rats	Active	Andrade-Cetto et al., 2000
	ď	4 -O-p-D-glucoside	11.7	11.	d
Errobotrya Japonica	Kosaceae	Aqueous extract of the leaves	Kabbits	Weak activity	Koman-Kamos et al., 1991
Eucalyptus globulus	Myrtaceae	Aqueous extract of the leaves	Mice	Active	Ferez et al., 1984
Euphorbia prostata	Euphorbiaceae	Aqueous extract of the entire	Rabbits	Active	Alarcon-Aguilar et al., 1998
		piani			

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	Mice	Active	Roman-Ramos et al., 1991
		of the aerial parts			
		Hexane, methylene chloride,	Mice	Inactive	Roman-Ramos et al., 2001
		methanol and aqueous ext of			
		the nowers		:	
;		Aqueous ext of the leaves	Kabbits	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
<i>Opuntia</i> sp	Cactaceae	Stem powder	Humans	Inactive	Frati-Munari et al., 1987
Opuntia streptacantha	Cactaceae	Aqueous extract of the aerial	Humans	Active	Frati-Munari et al., 1989
•		parts			
		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

		E		· · · · · · · · · · · · · · · · · · ·	4
Salpianthus macrodontus	Nyctaginaceae	Leaves and stems - 1ype or	Kabbits	weak activity	Koman-Kamos et al., 1991
		extract not stated			
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	Rabbits	Active	Roman-Ramos et al., 1991
		and stems			
Tecoma stans	Bignoniaceae	Aqueous extract of the leaves	Rabbits	Weak activity	Roman-Ramos et al., 1991
		and stems			
		Aqueous extract of the leaves	Rats	Active	Aguilar et al., 1993
		Part used and type of extract	Rabbits	Inactive	Guerra, 1946
		not stated			
		Aqueous extract of the entire plant	Mice	Active	Perez et al., 1984
Teucrium cubense	Lamiaceae	Aqueous extract of the leaves	Rabbits	Weak activity	Roman-Ramos et al., 1991
		and stems			
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

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

CanadaPoaceaeAvena sativaPoaceaeFatsia horridaAraliaceaePanax quinquefoliusAraliaceaeRhus typhinaAnacardiaceaeUSAMalvaceaeAbutilon theophrastiLiliaceaeAllium sativumLiliaceaeAloe veraUmbelliferaeAnethum graveolensUmbelliferaeArachis hypogaeaFabaceaeAstragalus membranaceusFabaceaeAstragalus melimusChenopodiaceaeAvena sativaPoaceae	Gum powder Aqueous extract of the rootbark Saponin fraction of the roots Aqueous extract of the roots Ginsenoside Aqueous extract Seeds powder in ration Bulb powder in ration Part used and type of extract not stated Leaves powder Part used and type of extract not stated	Humans Rabbits Rats Humans Humans Rats and dogs Rats Rats In vitro cells In vitro cells In vitro cells In vitro cells	Active Active Weak activity Active Inactive Active Inactive Inactive Inactive Inactive	Braaten et al., 1991 Large et al., 1938 Martinez et al., 1984 Vuksan et al., 2000 Sievenpiper et al., 2003 Fortier, 1949 Dugan et al., 1990a Chi et al., 1982 Broadhurst et al., 2000 Herlihy et al., 1998
na sativa sia horrida ax quinquefolius s typhina tilon theophrasti um sativum thum graveolens um graveolens chis hypogaea agalus membranaceus	Gum powder Aqueous extract of the rootbark Saponin fraction of the roots Aqueous extract of the roots Ginsenoside Aqueous extract Seeds powder in ration Bulb powder in ration Part used and type of extract not stated Leaves powder Part used and type of extract not stated Part used and type of extract	Humans Rabbits Rats Humans Humans Rats and dogs Rats Rats In vitro cells In vitro cells In vitro cells	Active Active Weak activity Active Inactive Active Inactive Inactive Inactive Inactive	Braaten et al., 1991 Large et al., 1938 Martinez et al., 1984 Vuksan et al., 2000 Sievenpiper et al., 2003 Fortier, 1949 Dugan et al., 1990a Chi et al., 1982 Broadhurst et al., 2000 Herlihy et al., 1998
ax quinquefolius ax quinquefolius s typhina tilon theophrasti um sativum twe graveolens um graveolens chis hypogaea agalus membranaceus plex halimus	Aqueous extract of the roots Saponin fraction of the roots Aqueous extract of the roots Ginsenoside Aqueous extract Seeds powder in ration Bulb powder in ration Part used and type of extract not stated Leaves powder Part used and type of extract not stated	Kabbits Rats Humans Humans Rats and dogs Rats Rats In vitro cells In vitro cells In vitro cells	Active Weak activity Active Active Active Inactive Inactive Inactive	Large et al., 1938 Martinez et al., 1984 Vuksan et al., 2000 Sievenpiper et al., 2003 Fortier, 1949 Dugan et al., 1990a Chi et al., 1982 Broadhurst et al., 2000 Herlihy et al., 1998
ax quinquefolius s typhina tilon theophrasti um sativum thum graveolens um graveolens chis hypogaea agalus membranaceus plex halimus	Saponin fraction of the roots Aqueous extract of the roots Ginsenoside Aqueous extract Seeds powder in ration Bulb powder in ration Part used and type of extract not stated Leaves powder Part used and type of extract not stated Part used and type of extract not stated Part used and type of extract	Rats Humans Humans Rats and dogs Rats In vitro cells Rats In vitro cells In vitro cells	Weak activity Active Inactive Active Inactive Inactive Inactive Inactive Inactive	Martinez et al., 1984 Vuksan et al., 2000 Sievenpiper et al., 2003 Fortier, 1949 Dugan et al., 1990a Chi et al., 1982 Broadhurst et al., 2000 Herlihy et al., 1998
s typhina tilon theophrasti um sativum thum graveolens um graveolens chis hypogaea agalus membranaceus	Aqueous extract of the roots Ginsenoside Aqueous extract Seeds powder in ration Bulb powder in ration Part used and type of extract not stated Leaves powder Part used and type of extract not stated Part used and type of extract not stated Part used and type of extract not stated	Humans Humans Rats and dogs Rats Rats In vitro cells In vitro cells In vitro cells	Active Active Active Inactive Inactive Inactive Inactive	Vuksan et al., 2000 Sievenpiper et al., 2003 Fortier, 1949 Dugan et al., 1990a Chi et al., 1982 Broadhurst et al., 2000 Herlihy et al., 1998
s typhina tilon theophrasti um sativum e vera thum graveolens um graveolens chis hypogaea agalus membranaceus	Ginsenoside Aqueous extract Seeds powder in ration Bulb powder in ration Part used and type of extract not stated Leaves powder Part used and type of extract not stated Part used and type of extract not stated Part used and type of extract	Humans Rats and dogs Rats Rats In vitro cells Rats In vitro cells In vitro cells	Inactive Active Active Inactive Inactive Inactive Inactive	Sievenpiper et al., 2003 Fortier, 1949 Dugan et al., 1990a Chi et al., 1982 Broadhurst et al., 2000 Herlihy et al., 1998
s typhina tilon theophrasti um sativum e vera thum graveolens chis hypogaea agalus membranaceus plex halimus	Aqueous extract Seeds powder in ration Bulb powder in ration Part used and type of extract not stated Leaves powder Part used and type of extract not stated Part used and type of extract not stated	Rats and dogs Rats Rats In vitro cells Rats In vitro cells In vitro cells In vitro cells	Active Active Inactive Inactive Inactive Inactive	Fortier, 1949 Dugan et al., 1990a Chi et al., 1982 Broadhurst et al., 2000 Herlihy et al., 1998 Broadhurst et al., 2000
tilon theophrasti um sativum e vera thum graveolens um graveolens chis hypogaea agalus membranaceus	Seeds powder in ration Bulb powder in ration Part used and type of extract not stated Leaves powder Part used and type of extract not stated Part used and type of extract not stated	Rats Rats In vitro cells In vitro cells In vitro cells In vitro cells	Active Inactive Inactive Inactive	Dugan et al., 1990a Chi et al., 1982 Broadhurst et al., 2000 Herlihy et al., 1998 Broadhurst et al., 2000
aceus	Bulb powder in ration Part used and type of extract not stated Leaves powder Part used and type of extract not stated Part used and type of extract not stated	Rats In vitro cells Rats In vitro cells In vitro cells	Inactive Inactive Inactive Inactive	Chi et al., 1982 Broadhurst et al., 2000 Herlihy et al., 1998 Broadhurst et al., 2000
ns anaceus	Part used and type of extract not stated Leaves powder Part used and type of extract not stated Part used and type of extract not stated	In vitro cells Rats In vitro cells In vitro cells	Inactive Inactive Inactive	Broadhurst et al., 2000 Herlihy et al., 1998 Broadhurst et al., 2000
ns anaceus	Leaves powder Part used and type of extract not stated Part used and type of extract not stated	Rats In vitro cells In vitro cells	Inactive Inactive	Herlihy et al., 1998 Broadhurst et al., 2000
anaceus	Part used and type of extract not stated Part used and type of extract not stated	In vitro cells In vitro cells	Inactive	Broadhurst et al., 2000
anaceus	not stated Part used and type of extract not stated	In vitro cells		
anaceus	Part used and type of extract not stated	In vitro cells		
anaceus	not stated		Inactive	Broadhurst et al., 2000
anaceus	Fart used and type of extract	In vitro cells	Week activity	Broadhurst et al., 2000
oranaceus	not stated			`
	Part used and type of extract	In vitro cells	Week activity	Broadhurst et al., 2000
	not stated	;		,
	Part used and type of extract not stated	In vitro cells	Inactive	Broadhurst et al., 2000
	Brun powder	Pigs	Active	Knudsen et al., 1995
	Brun powder	Humans	Active	Hopewell et al., 1993
	Part used and type of extract	In vitro cells	Weak activity	Broadhurst et al., 2000
	not stated	;		
Brassica nigra Cruciferae	Part used and type of extract	In vitro cells	Inactive	Broadhurst et al., 2000
Bungaion olounono	Hot stated [Honol extract of the periol	Date	Activo	Dubin et al 1038
	parts	Man	New York	Duoin Ct al., 1720
Camellia sinensis Theaceae	Part used and type of extract	In vitro cells	Active	Broadhurst et al., 2000
	not stated			
	Leaves - Smoking	Humans	Inactive	Podolsky et al., 1971
Capsicum annum Solanaceae	Part used and type of extract	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	In vitro cells	Inactive	Broadhurst et al., 2000
		not stated			
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	In vitro cells	Active	Broadhurst et al., 2000
		not stated			
Сіппатотит verum	Lauraceae	Part used and type of extract	In vitro cells	Active	Broadhurst et al., 2000
		not stated			
Coffea arabica	Rubiaceae	Part used and type of extract not stated	<i>In vitro</i> 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	In vitro cells	Active	Broadhurst et al., 2000
		not stated			

Humulus lupulus	Cannabaceae	Colupulone	Mice	Active	Mannering et al., 1994
Ipomoea hederaceae	Convolvulaceae	Seeds powder	Rats	Active	Dugan et al., 1990
<u>İ</u> pomoea 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	Rats	Inactive	Williams et al., 1959
	;	plant			4
Momordica charantia	Cucurbitaceae	Fraction peptide MC-6	Rats	Active	Nag, 2000
		Fraction peptide MC-6.1	Rats Date	Active	Nag, 2000 Nag, 2000
		Fraction peptide MC-6.2	Rats	Active	Nag, 2000 Nag 2000
Morus indica	Moraceae	Aqueous extract of the leaves	Humans	Active	Andallu et al., 2001
<i>Myristica fragans</i>	Myristicaceae	Part used and type of extract	In vitro cells	Active	Broadhurst et al., 2000
		not stated			
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	In vitro cells	Active	Broadhurst et al., 2000
		not stated			
Ocimum sanctum	Labiatae	Aqueous extr. of the entire	Organism not stated	Active	Luthy; Martinez 1964
Origanum vulgare	Labiatae	Part used and type of extract	In vitro cells	Active	Broadhurst et al., 2000
		not stated			
Panax ginseng	Araliaceae	Part used and type of extract	In vitro cells	Week activity	Broadhurst et al., 2000
:	;	not stated	,		
Fanax quinquejolius	Araliaceae	Saponin fraction of the roots	Kats	Weak activity	Martinez et al., 1984
		not stated	III VIU O CEIIS	wear activity	Di dadiitii st et ai., 2000
Petroselinum crispum	Umbelliferae	Part used and type of extract	In vitro cells	Inactive	Broadhurst et al., 2000
•		not stated			
Pimenta officinalis	Myrtaceae	Part used and type of extract	In vitro cells	Active	Broadhurst et al., 2000
Pimninella anisum	Umbelliferae	not stated Part used and type of extract	In vitro cells	Inactive	Broadhurst et al., 2000
		not stated			
Piper nigrum	Piperaceae	Part used and type of extract	In vitro cells	Inactive	Broadhurst et al., 2000
		not stated			

Part used and type of extract In vitro cells not stated Part used and type of extract In vitro cells not stated Part used and type of extract In vitro cells not stated	Inactive	Broadhurst et al., 2000
	Inactive	Broadhurst et al., 2000
	Week activity	Broadhurst et al., 2000
Rats	Active	Dugan et al., 1990a
Leaves - Type of extract not Dogs	Inactive	White jr et al., 1994
	Active	Broadhurst et al., 2000
	Inactive	Nash, 1958
Aqueous extract of the entire Mice	Active	Keller et al., 1981
plant 3-Hydroxy-3-methyl-glutaric Mice	Active	Witherup; McLaughlin, 1995
))
Mice	Inactive	Witherup; McLaughlin, 1995
4',5,7-Trihydroxy-3,3',5',6- Mice	Inactive	Witherup; McLaughlin, 1995
tetramethoxy-7- O - β -D-		
'es	Inactive	Allen, 1927
Ethanol ext. of the leaves Dogs	Inactive	Allen, 1927
Aqueous extrac of the leaves Dogs	Inactive	Allen, 1927
Part used and type of extract In vitro cells	Week activity	Broadhurst et al., 2000
Rats	Inactive	Svoboda et al., 1964
Rats	Questionable	Svoboda et al., 1964
Rats	Moderated act.	Svoboda et al., 1964
Rats	Slight activity	Svoboda et al., 1964
Rats	Inactive	Svoboda et al., 1964
Rats	Inactive	Svoboda et al., 1964
Rats	Questionable	Svoboda et al., 1964
Rats	Inactive	Svoboda et al., 1964
Rats	Slight activity	Svoboda et al., 1964
Rats	Moderated act.	Svoboda et al., 1964
Part used and type of extract In vitro cells	Inactive	Broadhurst et al., 2000
		,
	Active	Turner et al., 1974
prant Part used and type of extract In vitro cells	Week activity	Broadhurst et al., 2000
not stated Ethanol extract of the entire plant Part used and type of extract		Rabbits In vitro cells

REFERENCES

- Acosta-Patino JL, Jimenez-Balderas E, Juarez-Oropeza MA,
 Diaz-Zagoya JC 2001. Hypoglycemic action of
 Cucurbita ficifolia on Type 2 diabetic patients
 with moderately high blood glucose levels. J
 Ethnopharmacol 77: 99-101.
- Aguilar LC, Macias S, Chagoya A, Cardenas A, Diaz P, Cantu

 JM 1993. Antidiabetic activity of *Tecoma stans* in rats *Fitoterapia 64*: 304.
- Alarcon-Aguilar FJ, Roman-Ramos R, Jimenez-Estrada M, Reyes-Chilpa B, Gonzalez-Paredes, Flores-Saenz JL 1997. Effects of three Mexican medicinal plants (Asteraceae) on blood glucose levels in healthy mice and rabbits. *J Ethnopharmacol* 55: 171-77.
- Alarcon-Aguilar FJ, Roman-Ramos R, Perez-Gutierrez S, Aguilar-Contreras A, Contreras-Weber CC, Flores-Saenz JL 1998. Study of the anti-hyperglycemic effect of plants used as antidiabetics. *J Ethnopharmacol* 61: 101-110.
- Alarcon-Aguilar FJ, Jimenez-Estrada M, Reyes-Chilpa R, Roman-Ramos R 2000. Hypoglycemic effect of extracts and fractions from *Psacalium decompositum* in healthy and alloxan-diabetic mice. *J Ethnopharmacol 72*: 21-27
- Alarcon-Aguilar FJ, Hernández-Galicia E, Campos-Sepulveda AE, Xolalpa-Molina S, Rivas-Vilchis JF, Vasquez-Carrillo LI, Roman-Ramos R 2002a. Evaluation of the hypoglycemic effect of *Cucurbita ficifolia* Bouche (Curcurbitaceae) in different experimental models. *J Ethnopharmacol* 82: 185-189.
- Alarcon-Aguilar FJ, Campos-Sepulveda AE, Xolalpa-Molina S, Hernández-Galicia E, Roman-Ramos R 2002b. Hypoglycaemic activity of *Ibervillea sonorae* roots in healthy and diabetic mice and rats. *Pharma Biol* 40: 570-575.
- Alarcon-Aguilar FJ, Roman-Ramos R, Flores-Saenz JL, Aguirre-Garcia F 2002c. Investigation on the hypoglycaemic effects of extracts of four Mexican medicinal plants in normal and alloxan-diabetic mice *Phytother Res* 16: 383-386.
- Allen FM 1927. Blueberry leaf extract physiologic and clinical properties in relation to carbohydrate metabolism. *J Am Med Ass* 89: 1577-1581.
- Almeida RN, Barbosa-Filho JM, Naik SR 1985. Chemistry and pharmacology of an ethanol extract of *Bumelia sartorum*. *J Ethnopharmacol* 14: 173-185.
- Almeida RN, Agra MF 1986. Levantamento bibliográfico da flora medicinal de uso no tratamento da diabetes e alguns resultados experimentais. *Rev Bras Farm* 67: 105-110.
- Almeida RN, Navarro DS, Barbosa-Filho JM 2001. Plants with central analgesic activity *Phytomedicine 8*: 310-322
- Alvares M, Bazzone RB, Godoy GL, Cury R, Botion LM 1981. Hypoglycemic effect of *Stevia rebaudiana* Bertoni *I Brazilian Seminar on Stevia rebaudiana* 25-26.
- Andallu B, Suryakantham V, Srikanthi BL, Reddy GK 2001.

 Effect of mulberry (*Morus indica* L.) therapy on plasma and erythrocyte membrane lipids in patients with type 2 diabetes. *Clin Chim Acta 314*: 47-53.
- Andrade-Cetto A, Wiedenfeld H, Revilla MC, Sergio IA 2000. Hypoglycemic effect of Equisetum myriochaetum

- aerial parts on streptozotocin diabetic rats. *J Ethnopharmacol* 72: 129-133.
- Andrade-Cetto A, Wiedenfeld H 2001. Hypoglycemic effect of <u>Cecropia obtusifolia</u> on streptozotocin diabetic rats. <u>J Ethnopharmacol</u> 78: 145-149.
- Arduino F, Soares MLNG 1951. Hypoglycemic action of Anacardium occidentale (Cashew) in normal individuals Brazil Med 65: 305-308.
- Araújo IML 1999. Avaliação do efeito hipoglicemiante da Citrullus vulgaris Schrad (Melancia) em indivíduos diabéticos tipo 2 e normais. João Pessoa, 188p. Dissertação de Mestrado. Universidade Federal da Paraíba
- Avellar ME, Díaz A, Garcia I 1991. Evaluation de la medicina tradicional: efectos de *Cajanus cajan* L. (Guandu) y de *Cassia fistula* L. (Canafistula) en el metabolismo de los carbohidratos en el ratón. *Rev Méd Panamá* 16: 39-45.
- Aybar MJ, Riera ANS, Grau A, Sanchez SS 2001. Hypoglycemic effect of the water extract of *Smallantus sonchifolius* (yacon) leaves in normal and diabetic rats. *J Ethnopharmacol* 74: 125-132.
- Bailey CJ, Day C 1989. Traditional plant medicines as treatments for diabetes. *Diabetes Care 12*: 553-564.
- Bailey CJ, Day C, Turner SL, Leatherdale BA 1985. Cerasee, a traditional treatment for diabetes. Studies in normal and streptozotocin duabetic mice. *Diabetes Res* 2: 81-84
- Barbosa WLR, Santos WRA, Pinto LN, Tavares ICC 2002. Flavonóides de *Cissus verticillata* e a atividade hipoglicemiante do chá de suas folhas. *Rev Bras Farmacogn* 12(Supl 1): 13-15.
- Barceló A, Aedo C, Rajpathak S, Robles S 2003. The cost of diabetes in Latin America and the Caribbean. *Bull WHO 81*: 19-27.
- Basnet P, Kadota S, Terashima S, Shimizu M, Namba T 1993.

 Two new 2-arylbenzofuran derivatives from hypoglycemic activity-bearing fractions of *Morus insignis*. Chem Pharm Bull. 41: 1238-1243.
- Beltrame FL, Sartoretto JL, Bazotte RB, Cuman RN, Cortez DAG 2001. Phytochemical study and evaluation of the antidiabetic potential of *Cissus sicydides* L. (Vitaceae). *Quim Nova 24*: 783-785.
- Bischoff F, Long ML, Sahyun M 1929. Investigations of the hypoglucemic properties of reglykol pancreapatine and papaw. *J Pharmacol Exp Ther* 36: 311-312.
- Braaten JT, Wood PJ, Scott FW, Riedel KD, Poste LM, Collins

 MW 1991. Oat gum lowers glucose and insulin

 after an oral glucose load. *Amer J Clin Nutr 53*:

 1425-1430.
- Bresciani LFV, Yunes RA, Burger C, De Oliveira LE, Bof KL, Cechinel V 2004. Seasonal variation of kaurenoic acid, a hypoglycemic diterpene present in *Wedelia paludosa* (*Acmela brasiliensis*) (Asteraceae). *Z. Naturforschung C 59*: 229-232.
- Bressler R 1976. The unripe akee forbidden fruit. N Engl J Med 295: 500-501.
- Broadhurst CL, Polansky MM, Anderson RA 2000. Insulin-like biological activity of culinary and medicinal plant aqueous extracts *in vitro*. *J Agric Food Chem 48*: 849-852.
- Camargo MF, Lacerda AJB, Teixeira IPB, Martins DTO, Kawashita NH (2002). Efeito do tratamento de ratas

408

- diabéticas com extrato bruto da planta *Echinodorus* macrophyllys Micheli (Chapéu-de-couro). XVII Simpósio de Plantas Medicinais do Brasil, Cuiabá, MT. Brazil.
- Cardoso FV, Andrade NED, Lima ACSF, Longhi DT, Brigido AO, Marcucci MC, Scremin A, Paulino NI 2002. Avaliação da atividade dos extratos de plantas utilizadas na medicina popular para o tratamento da diabetes, sobre os canais de potássio modulados por ATP (KATA). XXXIV Congresso Brasileiro de Farmacologia e Terapêutica Experimental, Águas de Lindóia, SP, Brazil, p.215.
- Cartland, GF, Heyl FW, Neupert EF 1931. The hypoglycemic properties of white snakeroot (*Eupatorium urticaefolium*). J Amer Pharm Ass 20: 448-449.
- Carvalho ES, Araújo KGL, Rocha L, Lúcio EMRA, Sharapin N, Kaplan MAC 2002. Efeito dos extratos metanólico e aquoso das partes aéreas de *Bidens pilosa* L. em alfa-glicosidase. *XVII Simpósio de Plantas Medicinais do Brasil*, Cuiabá, MT, Brazil, FT.136.
- Chi MS, Koh ET, Stewart TJ 1982. Effects of garlic on lipid metabolism in rats fed cholesterol or lard. *J Nutr* 112: 241-248.
- Cuellar A, Estévez P 1980. A phytochemical study of Cuban plants. *Rev Cubana Farm 14*: 63-68.
- Damasceno DC, Volpato GT, Calderon I.MP, Rudge MVC 2002a. Estudos dos extratos de folhas de *Averrhoa carambola* e *Eugenia jambolana*, obtidas em farmácia de manipulação, sobre o diabete experimental. *Rev Bras Toxicol 15*: 9-14.
- Damasceno DC, Lima PHO, Galhiane MS, Volpato GT, Rudge MVC 2002b. Avaliação do efeito hipoglicemiante da sapogenina extraida de sementes de *Eugenia jambolana* Lam. *Rev Bras Pl Med 4*: 46-54.
- De Aguiar JC, Lins LJC 1958. Hypoglycemic action of inner bark (bast) of cashew tree (*Anacardium occidentale*). I. Action of a decoction on normal rats. *Anais Fac Med Univ Recife 18*: 193-197.
- Deas-Rodriguez M, Menéndez R, Alvarez A, González R (1988)

 Efecto hipoglicemiante de la albahaca morada /

 Hypoglycemic effect of Ocymun Sanctum L Rev

 Cuba Invest Bioméd 7: 53-9
- Deas-Rodriguez M, Seuc-Jo A, González-Suárez RM 1997.

 Estudio del efecto hipoglicemiante del *Ocimun sanctum* L. (albahaca-morada) con el uso de un ensayo biológico en ratones. *Rev Cuba Plantas Med* 2: 15-18.
- Derivi SCN, Mendez MHM, Rodrigues MCR, Fernandes ML, Silva MF 1987. Ação da fibra solúvel pectina sobre os níveis glicêmicos em ratos. *Rev Bras Farm* 68: 1-7.
- Diaz J, Durruty P, Tapia JC, Carrasco E, Riesco V, Durruty G, Garcia-de-los-Rios M 1990. Effect of dietary fiber in patients with noninsulin dependent diabetes-mellitus. *Rev Med Chil* 118: 24-32.
- Dubin HE, Corbitt HB 1928. Hypoglucemia-producing substance. Patent US 1,653,452.
- Dugan GM, Gumbmann MR 1990a. Toxicological evaluation of sicklepod and black nightshade seeds in short-term feeding studies in rats. Food Chem Toxicol 28: 101-107.
- Dugan GM, Gumbmann MR 1990b. Toxicological evaluation of morning glory seed: subchronic 90-day feeding

- study. Food Chem Toxicol 28: 553-559.
- Dugan GM, Gumbmann MR 1990a. Toxicological and nutritional evaluation of velvetleaf seed: subchronic 90-day feeding study and protein efficiency ratio assay. Food Chem Toxicol 28: 95-99.
- Ernest E 1997. Plants with hypoglycemic activity in humans. *Phytomedicine 4*: 73-78.
- Farias RAF, Rao VSN, Viana GSB, Silveira ER, Maciel MAM, Pinto AC 1997. Hypoglycemic effect of transdehydrocrotonin, a nor-clerodane diterpene from Croton cajucara. Planta Med 63: 558-560.
- Ferro E, Schinini A, Maldonado M, Rosner J, Schmeda-Hirschmann G 1988. Eugenia uniflora leaf extract and lipid metabolism in cebus apella monkeys. J Ethnopharmacol 24: 321-325.
- Fortier G 1949. Antidiabetic properties of *Rhus typhina*. Naval Med 14: 477-506.
- Frati-Munari AC, Castillo-Insunza MR, Riva-Pinal H, Ariza-Andraca CR, Banales-Ham M 1985. Effect of Plantago psyllium mucilage on the glucose tolerance test. Arch Invest Med (Mex) 16: 191-197.
- Frati-Munari AC, Yever-Garces A, Islas-Andrade S, Ariza-Andraca CR, Chavez-Negrete A 1987. Studies on the mechanism of hypoglycemic effect of nopal (Opunita sp.). Arch Invest Med (Mex) 18: 7-12.
- Frati-Munari, AC, Altamirano BE, Rodriguez-Barcenas N, Ariza-Andraca R, Lopez-Ledesma R 1989. Hypoglucemic effect of *Opuntia streptacantha* Lemaire: research with crude extracts. *Rev Archiv Invest Med (Mex)* 20: 321-322.
- Frati-Munari, AC, Gordillo BE, Altamirano P, Ariza CR, Cortes-Franco R, Chavez-Negrete A 1990. Acute hypoglycemic effect of *Opuntia streptacantha* Lemaire in niddm. *Diabetes Care 13*: 455-456.
- Frati-Munari AC, Roca-Vides R, Lopez-Perez RJ, De-Vivero I, Ruiz-Velazco M 1991. Glycemia index of several foods in Mexico. *Gac Med Mex 127*: 163-171.
- Galletto R, Siqueira VLD, Silva GEC, Nascimento KF, Bazotte RB 2003. XXXV Congresso Brasileiro de Farmacologia e Terapêutica Experimental, Águas de Lindóia, SP, Brazil, p. 203.
- Gallo FN 1941. Action of extract of *Bauhinia candicans* on normal blood sugar and experimental diabetes of dogs. *Rev Soc Argent Biol* 17: 128.
- Gómez R, Cervi FL, Guntzel C, Maslinkiewicz A, Barros HMT 2000. Curva glicêmica e variação de peso pelo extrato de erva de passarinho (*Phrygilanthus acutifolius*) em ratos. XV Reunião Anual da Federação de Sociedades de Biologia Experimental, Caxambu, MG, Brazil, p. 217.
- Gonalons GP, Fontana A 1926. Effect of *Phyllanthus sellowianus* on blood-sugar concentration. *Arch Argent Enferm Apar Digest Nutr* 993.
- Gonçalves MCR, Moura LSA, Rabelo LA, Barbosa-Filho JM, Cruz HMM, Cruz J 2000. Produtos naturais inibidores da enzima HMG CoA redutase. *Rev Bras Farm 81*: 63-71.
- Gonzalez-Mujica F, Motta N, Márquez AH, Capote-Zulueta J 2003. Effects of *Bauhinia megalandra* aqueous leaf extract on intestinal glucose absorption and uptake by enterocyte brush border membrane vesicles. *Fitoterapia 74*: 84-90.
- Grindley PBA, Omoruyi F, Asemota HN, Morrison EYSA 2002.

- Carbohydrate digestion and intestinal ATPases in streptozotocin-induced diabetic rats fed extract of yam (*Dioscorea cayenensis*) or dasheen (*Colocasia esculenta*). Nutri Res 22: 333-341.
- Grover JK, Yadav S, Vats V 2002. Medicinal plants of India with anti-diabetic potential. *J Ethnopharmacol 81*: 81-100.
- Guerra F 1946. The pharmacology of mexican antidiabetic plants. I. Action of *Tecoma mollis* on normal and diabetic blood sugar levels. *Rev Inst Salubridad y Enfermedad Trop (Mex)* 7: 237-248.
- Guerra F 1947. The pharmacology of Mexican antidiabetic plants. II. Action of *Coutarea latiflora* on normal and diabetic blood-sugar levels. *Rev Inst Salubridad* y Enfermedad Trop (Mex) 8: 29-38.
- Guerra RLL, Padton MCV, Rivas R, Blanco JCC, Parets MH, Gallardo AIA 2001. Efectos de un extracto hidroalcoholico de *Bidens alba* en ratas normales y con diabetes aloxanica. *Acta Farm Bonaerense 20*: 89-93.
- Gupta MP, Solis NG, Esposito-Avella M, Sanchez C 1984.

 Hypoglycemic activity of *Neurolaena lobata* (1.)

 R.Br. *J Ethnopharmacol 10*: 323-327.
- Handa SS, Chawla AS 1989. Hypoglycaemic plants A review. *Fitoterapia 60*: 195-224.
- Herlihy JT, Kim JD, Kalu DN, Nelson JF, Ward WF, Ikeno Y, Yu
 BP 1998. Effects of *Aloe vera* ingestion in the rat. II.
 Hormonal and metabolic characteristics. *Phytother Res* 12: 355-360.
- Hnatysyzn O, Mino J, Gorzalczany S, Ferraro G, Coussio J, Acevedo C 1997. Antidiabetic activity of *Phyllanthus sellowianus* in streptozotocin-induced diabetic rats. *Phytomedicine* 4: 251-253.
- Hnatyszyn O, Mino J, Ferraro G, Acevedo C 2002. The hypoglycemic effect of *Phyllanthus sellowianus* fractions in streptozotocin-induced diabetic mice. *Phytomedicine* 9: 556-559.
- Hopewell R, Yeater R, Ullirich I 1993. Soluble fiber: effect on carbohydrate and lipid metabolism. *Progress Food Nutr Sci 17*: 159-182.
- Ibanez-Camacho R, Meckes-Lozoya M, Mellado-Campos V 1983. The hypoglucemic effect of *Opuntia streptacantha* studied in different animal experimental models. *J Ethnopharmacol* 7: 175-181.
- <u>Ibanez-Camacho R, Roman-Ramos R 1979. Hypoglycemic</u> <u>effect of *Opuntia cactus. Arch Invest Med (Mex)*</u> <u>10: 223-230.</u>
- Ishii EL, Bracht A 1985. Ação do isosteviol e do steviol sobre o metabolismo de carboidratos em figado de rato perfundido isoladamente. Rev Unimar 7: 97-121
- Ivorra MD, Paya M, Villar A 1989. A review of natural products and plants as potential anti-diabetic drugs. *J Ethnopharmacol* 27: 243-275.
- Jelliffe DB, Stuart KL 1954. Acute toxic hypoglycaemia in the vomiting sickness of Jamaica. *Brit Med J 1*: 75-77.
- Juliant C. 1931. The hypoglucemic action of unha de vacca (Bauhinia fortificats). Rev Sud Amer Endocrinol Immunol Quimioter 14: 325-327.
- Kanegusuku M, Benassi JC, Pedrosa RC, Yunes RA, Cechinel-Filho V, Maia AA, .Souza MM, Delle-Monache F, Niero R 2002. Cytotoxic, hypoglycemic activity and phytochemical analysis of *Rubus imperialis*

- (Rosaceae). Z Naturforschung C 57: 272-276.
- Kean EA 1975. Hypoglycin. Academic press, New York.
- Keller WJ, Bourn WM, Bonfiglio JFA 1981. A folk medicine for diabetes mellitus. *Q J Crude Drug Res 19*: 49-51.
- Kerr D, Sherwin RS, Pavalkis F, Fayad PB, Sikorski L, Rife F,

 Tamborlane WV, During MJ 1993. Effect of caffeine
 on the recognition of and responses to hypoglycemia
 in humans. *Ann Intern Med 119*: 799-804.
- Knudsen KEB, Johansen HN 1995. Mode of action of oat bran in the gastrointestinal tract. *Eur J Clin Nutr 49*: S163-S169.
- Kono S, Aynehchi S, Dolin DJ, Schwartz AM, Choudhury MS, Tazaki H 2002. Anticancer and hypoglycemic effects of polysaccharides in edible and medicinal maitake mushroom (*Grifola frondosa* (Dicks.: Fr.) S. F. Gray). *Inter J Med Mushrooms 4*: 185-195.
- Krenisky JM, Luo J, Reed MJ, Carney JR 1999. Isolation and antihyperglycemic activity of bakuchiol from *Otholobium pubescens* (Fabaceae), a peruvian medicinal plant used for the treatment of diabetes. *Biol Pharm Bull 22*: 1137-1140.
- Kudolo GB 2001. The effect of 3-month ingestion of *Ginkgo biloba* extract (EGb 761) on pancreatic betacell function in response to glucose loading in individuals with non-insulin-dependent diabetes mellitus. *J Clin Pharmacol* 41: 600-611.
- Lamba SS, Buch KY, Lewis H, Lamba HJ 2000. Phytochemicals as potential hypoglycemic agents. *Studies in Natural Products Chemistry*, 21: 457-495.
- Large RG, Brocklesby HN 1938. A hypoglycemic substance from the roots of the devil's club (*Fatsia horrida*). *Can Med Ass J 39*: 32-35.
- Lemus I, Garcia R, Jabsa Z, Erazo S, Garcia H 1986. Hypoglycemic activity of an extract of *Bauhinia* candicans B. Plant Med Phytother 20: 8-17.
- Lemus I, Garcia R, Delvillar E, Knop G 1999. Hypoglycaemic activity of four plants used in Chilean popular medicine. *Phytother Res* 13: 91-94.
- Longhi DT, Ballmann JD, Brigido AO, Marcucci MC, Scremin A, Paulino N 2003. Mechanisms involved in the hypoglicemic effect of ethanolic extract of *Polymnia sonchifolia* Poepp. & Endl. *XXXV Congresso Brasileiro de Farmacologia e Terapêutica Experimental*, Águas de Lindóia, SP, Brazil, p. 226
- Lores RI, Pujol MC 1990. *Petiveria alliaceae* L. (Anamu).

 Study of the hypoglycemic effect. *Med Interne 28*: 347-352.
- Luthy N, Martinez-Fortun O 1964. A possible oral hypoglycemic factor in abahaca morada (*Ocimum sanctum*). *Ohio J. Sci. 64*: 223-224.
- Mannering GJ, Shoeman JA, Shoeman DW 1994. Effects of colupulone, a component of hops and brewers-yeast, and chromium on glucose-tolerance and hepatic cytochrome-P450 in nondiabetic and spontaneously diabetic mice. *Bioch Biophys Res Comm 200*: 1455-1462.
- Manrique JFM, Sousa YMA, Lima FO, Vasconcellos MC, Borras MRL, Ferreira LCL, Costa PRC, Roland IA 2002. Efeito do extrato aquoso de *Brosimum acutifolium* sobre os níveis plasmátaticos de glicose, colesterol e triglicerídeod em ratos wistar. XVII Reunião Anual da Federação de Sociedades

- de Biologia Experimental, Caxambu, MG, Brazil, p. 20.085.
- Marles RJ, Farnsworth NR 1995. Antidiabetic plants and their active constituents. *Phytomedicine* 2: 137-189.
- Martinez B, Staba EJ 1984. The physiological effects of aralia, panax and eleutherococcus on exercised rats. *Jap J Pharmacol* 35: 79-85.
- Matsumura T, Kasai M, Hayashi T, Arisawa M, Momose Y, Arai I, Amagaya S, Komatsu Y 2000. Alpha-glucosidase inhibitors from Paraguayan natural medicine, nangapiry, the leaves of *Eugenia uniflora*. *Pharma Biol* 38: 302-307.
- Meckes-Lozoya M, Campos VM 1986. Pharmacological screening of Mexican plants, popularly used for the treatment of cough. *Fitoterapia* 57: 365-370.
- Mellado V, Lozoya M 1984. Effect of the aqueous extract of Cecropia obtusifolia on the blood sugar of normal and pancreatectomized dogs. Int J Crude Drug Res 22: 11-16.
- Menaul P. 1923. The physiological effect of gossypol. *J Agr Res* 26: 233-224.
- Mills J, Melville GN, Bennett C, West M, Castro A 1987. Effect of hypoglycin-A on insulin release. *Biochem Pharmacol* 36: 495-497.
- Miron VR, Mazzanti CM, Schossler DRC, Filappi A, Prestes D, Balz D, Morsch A, Cecim M, Schetinger MRC, Morsch VM, Neu TN 2002. Extrato da casca de *Syzygium cumini* na glicemia e estresse oxidativo de ratos normais e diabéticos. *XVII Reunião Anual da Federação de Sociedades de Biologia Experimental*, Caxambu, MG, Brazil, p. 16.008.
- Morais LCSL, Barbosa-Filho JM, Almeida RN 2003. Plants and bioactives compounds for the treatment of Parkinson's desease. *Arquivo de Fitomedicina 1*: 127-132.
- Morato GS, Calixto JB, Cordeiro L, De-Lima TCM; Morato EF, Nicolau M, Era GA, Takahashi RN, Valle RMR, Yunes RA 1989. Chemical and pharmacological studies on *Talauma ovata* St. Hil. (Magnoliaceae). *J Ethnopharmacol* 26: 277-286.
- Mori T, Nishikawa Y, Takata Y, Kashiuchi N, Ishihara N 2001. Effect of insulina leaf extract on development of diabetes. Comparison between normal, streptozotocin-induced diabetic rats and hereditary diabetic mice. *Nippon Eiyo Shokuryo Gakkaishi 54*: 197-203.
- Morrison EY, West ME 1982. A preliminary study of the effects of some West Indian medicinal plants on blood sugar levels in the dog. *West Indian Med J 31*: 194-197.
- Morrison EY, West ME 1985. The effect of *Bixa orellana* (annatto) on blood sugar levels in the anaesthetized dog. *West Indian Med J 34*: 38-42.
- Moura MD, Torres AR, Oliveira RAG, Diniz MFFM, Barbosa-Filho JM 2001. Natural products inhibitors of models of mammary neoplasia. *Brit J Phytotherapy* 5: 124-145.
- Moura MD, Silva JS, Oliveira RAG, Diniz MFFM, Barbosa-Filho JM 2002. Natural products reported as potential inhibitors of uterine cervical neoplasia. *Acta Farm Bonaerense* 21: 67-74.
- Nag B 2000. Orally active fraction of *Momordica charantia*, active peptides thereof, and their use in the treatment

- of diabetes. Patent US 6,127,338 p.1-11.
- Naik SR, Barbosa-Filho JM, Dhuley JN 1991. Probable mechanism of hypoglycemic activity of bassic acid, a natural product iIsolated from *Bumelia sartorum*. *J Ethnopharmacol 33*: 37-44.
- Nash JB, Albers CC, Howard JK, Fly Jr SH 1958. Lack of antidiabetogenic and antidiabetic effects of *Tecoma* stans in oxan diabetes. Tex Rep Biol Med 8: 350-353.
- Neves RE, Menezes FS, Pereira NA, Moreira DL 2002.

 Avaliação farmacológica de plantas medicinais utilizadas como hipoglicemiantes na região do médio Paraíba do estado do Rio de Janeiro. XVII Simpósio de Plantas Medicinais do Brasil, Cuiabá, MT, Brazil, p. FT. 091.
- Novaes EP, Rossi C, Poffo C, Pretti E, Oliveira AE, Schlemper V, Niero R, Cechinel-Filho V, Burger C 2001.

 Preliminary evaluation of the hypoglycemic effect of some Brazilian medicinal plants. *Therapie 56*: 427-430.
- Oliveira ACP, Endringer DC, Coelho MM 2003. The starch from *Solanum lycocarpum* St. Hill. fruit is not a hypoglycemic agent. *Braz J Med Biol Res* 36: 525-530
- Oliveira F, Saito ML 1989. Alguns vegetais brasileiros empregados no tratamento da diabetes. *Rev Bras* Farm 2/4: 170-196.
- Oliveira AEA, Machado OLT, Gomes VM, Neto JX, Pereira AC, Vieira JGH, Fernandes KVS, Xavier J 1999. Jack bean seed coat contains a protein with complete sequence homology to bovine insulin. *Protein and Peptide Letters* 6: 15-21.
- Ospina LF, Olarte JE, Calle J, Pinzón R 1995. Comprobación de la actividad hipoglicemiante y captadora de radicales libres oxigenados de los principios activos de *Curatella americana* L. *Rev Colomb Ci Quim Farm 24*: 6-11.
- Oviedo CA, Fronciani G, Moreno R, Maas L 1970. Hypoglycemic action of *Stevia rebaudiana*. *Excerpta Medica 209*: 92-96.
- Pepato MT, Oliveira JR, Kettelhut IC, Migliorini RH 1993.

 Assessment of the antidiabetic activity of Myrcia
 uniflora extracts in streptozotocin-diabetic rats.

 Diabetes Res 22: 49-57.
- Pepato MT, Folgado VBB, Kettelhut IC, Brunetti IL 2001. Lack of antidiabetic effect of a *Eugenia jambolana* leaf decoction on rat streptozotocin diabetes. *Braz J Med Biol Res* 34: 389-395.
- Pepato MT, Keller EH, Baviera AM, Kettelhut IC, Vendramini RC, Brunetti IL 2002. Anti-diabetic activity of *Bauhinia forficata* decoction in streptozotocin-diabetic rats *J Ethnopharmacol 81*: 191-197.
- Pepato MT, Baviera AM, Vendramini RC, Perez MPMS, Kettelhutt IC, Brunett IL 2003. Cissus sicyoides (princess vine) in the long-term treatment of streptozotocin-diabetic rats. Biotechnol Appl Biochem 37(Part 1): 15-20.
- Pereira NA 1997. Plants as hypoglycemic agents. *Ciência e Cultura 49*: 354-358.
- Pereira JV, Modesto-Filho J, Agra MF, Barbosa-Filho JM 2002.

 Plant and plant-derived compounds employed in prevention of the osteoporosis. *Acta Farm Bonaerense* 21: 223-234.

- Perez RM, Ocegueda A, Muñoz JL, Ávila JG, Morrow WW 1984. A study of the hypoglucemic effect of some mexican plants. *J Ethnopharmacol* 12: 253-262.
- Perez RM, Perez S, Zavala MA, Perez C 1996. Effects of Agarista mexicana and Verbesina persicifolia on blood glucose level of normoglycaemic and alloxandiabetic mice and rats. Phytother Res 10: 351-353.
- Perez RM, Zavala MA, Vargas SR 1997. Coyolosa, a new hypoglycemic from *Acrocomia mexicana*. *Pharm Acta Helv 13*: 105-111.
- Perez RM, Perez C, Perez S, Zavala MA 1998a. Effect of triterpenoids of *Bouvardia terniflora* on blood sugar levels of normal and alloxan diabetic mice. *Phytomedicine* 5: 475-448.
- Perez RM, Zavala MA, Perez S, Perez C 1998b. Antidiabetic effect of compounds isolated from plants.

 Phytomedicine 5: 55-75.
- Perez RM, Cervantes H, Zavala MA, Sánchez SJ, Perez S, Perez C 2000a. Isolation and hypoglycemic activity of 5, 7,3'-trihydroxy-3,6,4'-trimethoxyflavone from *Brickellia veronicaefolia. Phytomedicine* 7: 25-29.
- Perez RM, Perez C, Zavala MA, Perez S, Hernandez H,
 Lagunes F 2000b Hypoglycemic effects of lactucin8-O-methylacrylate of *Parmentiera edulis* fruit. *J*Ethnopharmacol 71: 391-394.
- Perez RM, Ramirez E, Vargas R 2001. Effect of *Cirsium pascuarense* on blood glucose levels of normoglycaemic and alloxan-diabetic mice.

 Phytother Res 15: 552-554.
- Podolsky S, Pattavina CG, Amaral MA 1971. Effect of marijuana on the glucose-tolerance test. *Ann N Y Acad Sci 191*: 54-60
- Presta GA, Pereira NA 1987. Atividade de abageru, Chysobalanus icaco Lin. (Chrysobalanaceae) em modelos experimentais para o estudo de plantas hipoglicemiantes. Rev Bras Farm 68: 91-101.
- Provasi M, Oliveira CE, Martinho MC, Pessini LG, Bazotte RB, Cortez DAG 2001. Avaliação da toxicidade e do potencial antihiperglicemiante da *Averrhoa carambola* L. (Oxalidaceae). *Acta Sci. 23*: 665-669.
- Rahman AU, Zaman K 1989. Medicinal-plants with hypoglycemic activity. *J Ethnopharmacol* 26: 1-55.
- Reis JC, Oliveira APO, Soares FR, Brito SMRC 2002. Avaliação da atividade hipoglicemiante de *Vatairae* macrocarpa (Benth) Ducke em ratos. XVII Reunião Anual da Federação de Sociedades de Biologia Experimental, Caxambu, MG, Brazil, p. 20.091.
- Revilla MC, Andrade-Cetto A, Islas S, Wiedenfeld H 2002.

 Hypoglycemic effect of Equisetum myriochaetum
 aerial parts on type 2 diabetic patients. J
 Ethnopharmacol 81: 117-120
- Rivera G 1942. Preliminary chemical and pharmacological studies on "cundeamor", *Momordica charantia*. II. *Amer J Pharm 114*: 72-73.
- Rocha LG, Almeida JRGS, Macedo RO, Barbosa-Filho JM 2005.

 <u>A review of natural products with antileishmanial activity. *Phytomedicine 12*: 514-535.</u>
- Rodriguez J, Loyola C, Schmeda-Hirschmann G 1992.

 Hypoglycaemic activity of *Hexachlamys edulis*(yvahai) extract in rats. *Phytother Res 6*: 47-49.
- Rodriguez J, Loyola JI, Maulen G, Schmeda-Hirschmann G 1994. Hypoglycaemic activity of *Geranium core*-

- core, Oxalis rosea and Plantago major extracts in rats. Phytother Res 8: 372-374.
- Rojo-Domínguez D, Bell-Heredia L, Cansio-Martínez E, Iglesias-Lores R 2002. Efecto del extracto hipoglicemiante de *Petiveria alliacea* L sobre el consumo de glucosa por los eritrócitos. *Rev Cuba Invest Bioméd 21*: 161-166.
- Roman-Ramos R, Flores-Saenz JL, Partida-Hernandez G, Lara-Lemus A, Alarcon-Aguilar FJ 1991. Experimental study of hypoglycemic activity of some antidiabetic plants. *Arch Invest Med (Mex)* 22: 87-93.
- Roman-Ramos R, Contreras-Weber CC, Nohpal-Grajeda G, Flores-Saenz JL, Alarcon-Aguilar FJ 2001. Blood glucose level decrease caused by extracts and fractions from *Lepechinia caulescens* in healthy and alloxan-diabetic mice. *Pharma Biol* 39: 317-321.
- Russo EMK, Reichelt AA, De-Sá JR, Furlanetto RP, Moises RC, Kasamatsu TS, Chacra AR 1990. Clinicaltrial of *Myrcia uniflora* and *Bauhinia-forficata* leaf extracts in normal and diabetic-patients. *Braz J Med Biol Res* 23: 11-20.
- Salvado AC, Naranjo JP, Evseva EC, Royero RH, Rodríguez DLL 1997. Tamizaje, tecnologia, control de calidad y farmacologia del extracto fluido de *Bouganvillea* spectabilism Willd. Rev Cuba Plantas Med 2: 19-25
- Sampaio EDM, Furtado FDAS, Furtado MJS, Cavalcante MNNDS, Riedel ODO 1979. Hypoglycemic effect of raw coffee beans (*Coffea arabica* L. Rubiaceae). Rev Med Univ Fed Ceara 19: 49-53.
- Sievenpiper JL, Arnason JT, Leiter LA, Vuksan V 2003. Variable effects of American ginseng: A batch of American ginseng (*Panax quinquefolius* L.) with a depressed ginsenoside profile does not affect postprandial glycemia. *Eur J Clin Nutr* 57: 243-248.
- Silva FRMB, Szpoganicz MG, Pizzolatti MA, Willrich V, Sousa E 2002. Acute effect of *Bauhinia forficata* on serum glucose levels in normal and alloxan-induced diabetic rats. *J Ethnopharmacol* 83: 33-37.
- Silva JS, Moura MD, Oliveira RAG, Diniz MFFM, Barbosa-Filho JM 2003. Natural products inhibitors of ovarian neoplasia. *Phytomedicine* 10: 221-232.
- Silveira NA, Nascimento SDM, Ferreira JDJ, Carvalho OF, Paula JR 2001. Efeito do extrato etanólico de *Rudgea viburnioides* sobre a concentração plasmática de glicose, triglicérideos e colesterol em ratos Wistar. *XVI Reunião Anual da Federação de Sociedades de Biologia Experimental*, Caxambu, MG, Brazil, p. 318.
- Smith GW 1983. Arctic Pharmacognosia II. Devil's club, Oplopanax horridus. J Ethnopharmacol 7: 313-320.
- Sousa E, Zanatta L, Charão CCT, Seifriz I, Creczynski-Pasa TB, Pizzolatti MG, Szpoganicz B, Silva FRMB 2002a. Efeito hipoglicêmico e propriedades antioxidantes do kaempferol-3-7-O-diramnosideo isolado da fração butanólica da *Bauhinia forficata* Link. *XVII Simpósio de Plantas Medicinais do Brasil, Cuiabá, MT, Brazil*, p. FT.185.
- Sousa E, Cunha-Júnior A, Charão CCT, Zanatta L, Szpoganicz B, Pizzolatti MG, Jorge AP, Silva FRMB 2002b. Efeito agudo do extrato bruto de *Vitex megapotamica* (Verbenaceae) na glicemia de ratos normais,

- normais hiperglicêmicos e diabéticos induzidos com aloxana. VII Simpósio de Plantas Medicinais do Brasil, Cuiabá, MT, Brazil, p. FT.252.
- Souza-Formigoni MLO, Lodder HM, Ferreira TMS, Carlini EA

 1986. Pharmacology of lemongrass (*Cymbopogon citratus* Stapf). II. Effects of daily two month administration in male and female rats and in offspring exposed in utero. *J Ethnopharmacol* 17: 65-74.
- Svoboda GH, Gorman M, Root MA 1964. Alkaloids of *Vinca*rosea (Catharanthus roseus). 28. A preliminary
 report on hypoglycemic activity. Lloydia 27: 361363.
- Taylor TE, Molyneux ME, Wirima JJ, Fletcher KA, Morris K
 1988. Blood-glucose levels in Malawian children
 before and during the administration of intravenous
 quinine for severe falciparum-malaria. *N Engl J Med 319*: 1040-1047.
- Teixeira CC, Fuchs FD, Blotta RM, Knijnik J, Delgado IC, Netto MS, Ferreira E, Costa AP, Mussnich DG, Ranquetat GG, Castaldo G 1990. Effect of tea prepared from leaves of *Syzygium jambos* on glucose tolerance in nondiabetic subjects. *Diabetes Care 13*: 907-908.
- Teixeira CC, Pinto LP, Kessler FHP, Da-Paixão LQ, Miura CS, Guimarães MS, Miura MS, Gastaldo GJ, Fuchs FD 1998. Is the decoction of mango leaves an antihyperglycemic tea?. Fitoterapia 69: 165-168.
- Teixeira CC, Rava CA, Silva PM, Melchior R, Argenta R, Anselmi F, Almeida CRC, Fuchs FD 2000.

 Absence of antihyperglycemic effect of jambolan in experimental and clinical models. *J Ethnopharmacol* 71: 343-347.
- Tomas GE, Lock O, Jurupe H 1999. Chemical study and hypoglycemic and hypolipemic activity of *Gentianella thyrsoidea* Hooker. *Bol Soc Quim Peru* 65: 231-238.
- Tsiodras S, Shin RK, Christian M, Shaw LM, Sass DA 1999.

 Anticholinergic toxicity associated with lupine seeds as a home remedy for diabetes mellitus. *Ann Emerg Med 33*: 715-717.
- Turner CE, Craig Jr JC 1974. Hypoglycemic compound. *Patent US 3,922*,263 4pp.
- Vale DSD, MR. Kerntopf CK, Pontes MC, Fonteles M 2001. XVI Reunião Anual da Federação de Sociedades de Biologia Experimental, Caxambu, MG, Brazil, p. 319.
- Valencia JM, Villavicencio R, Vicuña P, Torres E 1994. Efecto agudo del *Aloe vera* Linneo y *Ciclanthera pedata*Shrad en ratas diabéticas. *Rev Med Peru 66*: 80-82.
- Volpato GT, Damasceno DC, Calderon IMP, Rudge MVC 1999. Study of *Bauhinia forficata* L. extract on diabete in pregnant rats. *Rev Bras Pl Med 2*: 49-55.
- Volpato GT, Damasceno DC, Calderon IMP, Rudge MVC 2002. Revisão de plantas brasileiras com comprovado efeito hipoglicemiante no controle do diabetes mellitus. *Rev Bras Pl Med 4*: 35-45.
- Von Schmeling GA, Varela-de-Carvalho F, Domingos-Espinosa A 1977. Cienc Cult (Brazil) 29: 599-600.
- Vuksan V, Stavro MP, Sievenpiper JL, Koo VY, Wong E, Beljan ZU, Francis T, Jenkins AL, Leiter LA, Josse-Robert G, Xu Z 2000. American giseng improves glycemia in individuals with normal glucose tolerance: Effect of dose and time escalation. J Am College Nutr 19:

- 738-744.
- Watters K, Blaisdell P 1989. Reduction of glycemic and lipid levels in db/db diabetic mice by *Psyllium* plant fiber. *Diabetes 38*: 1528-1533.
- White Jr JR, Kramer J, Campbell RK, Bernstein R 1994. Oral use of a topical preparation containing an extract of *Stevia rebaudiana* and the chrysanthemum flower in the management of hyperglycemia. *Diabetes Care 17*: 940-941.
- Williams RH, Martin FB, Henley ED, Swanson HE 1959.

 Inhibitors of insulin degradation. *Metabolism 8*: 99113.
- Witherup KM, McLaughlin JL, Judd RL, Ziegler MH, Medon PJ, Keller WJ 1995. Identification of 3-hydroxy-3-methylglutaric acid (HMG) as a hypoglycemic principle of Spanish moss (*Tillandsia usneoides*). *J Nat Prod 58*: 1285-1290.