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Review

Mexican plants with hypoglycaemic effect used in the treatment of diabetes

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Abstract

Diabetes mellitus is a syndrome which affects more and more people in all countries over the world. In México, it is commonly treated with herbal extracts. Such treatment may be of considerable benefit especially during the early stages of the illness. In this review, we discuss species commonly used in México in the treatment of diabetes. A total of 306 species have records of a popular use in the treatment of this syndrome in México. Seven of these species – *Cecropia obtusifolia* Bertol. (Cecropiaceae), *Equisetum myriochaetum* Schlecht & Cham (Equisetaceae), *Acosmium panamense* (Benth.) Yacolev (Fabaceae), *Cucurbita ficifolia* Bouché (Cucurbitaceae), *Agarista mexicana* (Hemsl.) Judd. (Ericaeae), *Brickellia veronicaefolia* (Kunth) A. Gray (Asteraceae), *Parmentiera aculeata* (*Kunth*) *Seem.* (Bignoniaceae) – are discussed in greater detail, highlighting our current knowledge about these botanicals, but also the enormous gaps in our knowledge, most notably as it relates to the species' toxicology, the pharmacokinetics of its active constituents and their metabolism.

Keywords: Type 2 diabetes; Hypoglycaemic plants; México; Neotropics; Traditional medicine

Contents

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1. Introduction

It is well known that diabetes mellitus is the commonest endocrine disorder that, according to the World Health Organization (WHO, 2004), affects more than 176 million people world wide, in México the WHO estimates that the number of diabetic patients will increase from more than 2 million in 2002 to more than 6 million in 2030, which would imply that in a few decades México may have highest rate of diabetes in the world. According to the Mexican health services, in 2001 diabetes was the first cause of mortality among the Mexican population (SSA, 2004). Because of the complications linked to diabetes like heart disease, retinopathy, kidney disease, and neuropathy, it also is a common cause of chronic morbidity and disability among the working population.

The term diabetes mellitus describes a metabolic disorder of multiple aetiologies and is characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The causes of type 2 diabetes are either insulin resistance with relative insulin deficiency or predominantly an insulin secretory defect with or with out insulin resistance (WHO, 1999).

From an ethnopharmacological perspective, it is important to understand that this disease is one at the interface of conventional biomedical and local (or traditional) treatment. In México, limited data is available but based on our field experience diabetic patients practically always use plants with or without biomedical medication. Normally, patients are diagnosed in one of the primary health care centres and the MDs in these centres normally also prescribe appropriate medication. However, once a diagnosis is made the patients often recur to either local healers or to vendors of herbal and other health care products. Thus this is a disease for which many of the 'traditional' treatments were in fact developed in the last decades by local healers. In USA, some plant based compounds as well as herbal remedies are used along with other medications. In some cases, patients used these treatments instead of conventional medications, and severe complications including increased hospitalizations, ketoacidosis, and acute hyperglycaemia occurred (Shane-Mc Whorter, 2001). In Germany, at least two products for the treatment of diabetes, based on Mexican medicinal plants are available: Hando, Nopal (opuntia sp.), manufactured by Hando Austria and Sucontral (Coplachi: Hintonia sp.) manufactured by Harras Pharma, Munich.

There have been many studies on hypoglycaemic plants and a great variety of compounds have been isolated (alkaloids, glycosides, terpenes, flavonoids, etc.), but the main bottleneck is the further development of such 'leads' into clinically useful medicines and especially phytomedicines or adequate nutritional supplements, which would be of direct benefits to patients. In this context, it is important to remember that the modern drug metformin (a bi**g**uanide) is a derivate of an active natural product, galegine a guanidine isolated from the plant *Galega officinalis* L., which was used in the medieval times to relieve the intense urination in diabetic people (Witters, 2001).

In this review we summarize information on plants with current information in the international literature and highlight the current state of ethnopharmacological, phytochemical and clinical research on some of the more widely used and better known species.

2. An overview of important sources of information on Mexican antidiabetic plants

Several valuable reviews on the ethnobotanical use of plants of México are available (Martínez, 1954; Díaz, 1976; Aguilar et al., 1994; Argueta, 1994; Aguilar and Xolalapa, 2002). Other data can be found in many of the ethnobotanical thesis or monographs on specific regions. For México, we have documented at least 306 species from 235 genera and 93 families used as hypoglycaemic agents (see Table 1). The most commonly mentioned families are: Asteraceae (47 sp.), Fabaceae, (27), Cactaceae (16), Solanaceae and Euphorbiaceae (10) and Laminaceae (9).

But in our own experience from field work in Guerrero (Andrade-Cetto, 1995), when a directed ethnobotanical study is performed looking only from hypoglycaemic plants instead of a broad study looking for all medicinal plants, this number is at least double. Therefore, we estimate that there are about 500 species used by Mexican people to treat type 2 diabetes.

Starting at the early 1990s, important pharmacological studies were conducted by Alarcón Aguilar and Román-Ramos (Alarcón-Aguilar et al., 1997, 1998, 2000a, 2000b, 2002a, 2002b; Román-Ramos et al., 1991, 2001). In the beginning, this group tested several plants for their pharmacological activity in temporarily hyperglycaemic rabbits. Hyperglycaemia was induced with a glucose charge; later on they use healthy and alloxan-diabetic mice. Normally, the plant was process in the traditional way and the water extract tested. The authors have not looked for bioactive compounds of these species, with the exception of a detailed report on the pharmacology and phytochemistry of *Psacalium* sp.

The group of Pérez-Gutiérrez et al. (1996, 1998a, 1998c, 2000a, 2000b, 2001), Pérez-Gutiérrez and Vargas (2001) and Pérez et al. (1984, 1992) normally look for the pharmacological activity in normal and alloxan diabetic mice and rats. The group isolated bioactive compounds from some of the species working with the chloroform extracts.

The group of Andrade-Cetto (Andrade-Cetto et al., 2000; Andrade-Cetto and Wiedenfeld, 2001, 2004, and Wiedenfeld et al., 2000, 2003) generally starts with their own field studies. Then the traditionally used extract (normally water or butanol) is tested on Streptozotocin diabetic rats, from the active extract the main compounds are isolated and tested in the animal model.

There are some clinical studies like the well known one by Frati-Munari et al. (1983, 1987, 1989a, 1989b, 1989c, 1990, 1991a, 1991b), Castaneda-Andrade et al. (1997), Acosta-Patino (2001) (Revilla-Monsalve et al., 2002), and (Herrera-Arellano et al., 2004). Acosta Patiño and Revilla associated with the above described groups.

Finally we have recompilations in which the authors describe some aspects of species with hypoglycaemic effects from México (Pérez-Gutiérrez et al., 1998b) or some Mexican plants as part of world wide studies (Marles and Farnsworth, 1995; Ernst, 1997; Lamba et al., 2000). The detailed reviews of Shane-Mc Whorter (2001) and Yeh et al. (2003) on clinical aspects of anti-diabetic plants include, for example, the commonly used *Momordica charantia* L. (originally from Asia) and *Opuntia* sp. (a native of México). These relatively well known studied species are excluded from this review. Also, "Matarique" *Psacalium decompositum* (*Gray*) *H.E. Robins* & *Brett*, is not reviewed here. Research and development activities on this botanical lead to a patent on some compounds present in the plant with hypoglycaemic proprieties A detailed review was conducted as part of the efforts to obtain a patent (Inman et al., 1998): "the novel hypoglycemically active eremophilanolide sesquiterpenes which can be

Table 1
Main plants reported in México as Hypoglycemic, the original table is from Andrade, 1995, the data were actualized and 40 species added from Aguilar and Xolalpa 2002, the correct botanical names were corroborated at Missouri Botanical Garden (2004)—TROPICOS

Scientific name	Common name	Family	Plant part used and preparation	Pharmacological STudies*	Phytochemical informat**
Abutilon lignosum (Cav.) D. Don	Sacxiu	Malvaceae	Root infusion		
Abutilon trisulcatum (Jacq.) Urban.	Tronadora	Malvaceae	Leaf boil		
Acacia retinodes Schltdl.	Mimosa	Fabaceae	Leaf boil		
Acourtia thurberi. (A. Gray) Reveal & R. M. King	Matarique	Asteraceae	Plant (aerial) infusion	Normal rabbits (+)	
Acrocomia mexicana Karw. ex Mart.	Coyol	Arecaceae	Root roasted, fruit raw	Alloxanic mice (+) Alloxanic mice (++) EtOH	Tetrahydropyrane, Coyolose
Agastache mexicana (Kunth) Lint et Epling	Toronjil	Lamiaceae	Plant (aerial) infusion		Essential oils
Agave atrovirens Karw. Ex Salm-Dyck	Maguey	Agavaceae	Steam macerated		Sapogeninns
Agave lecheguilla Torr.	Lechuguilla	Agavaceae	Steam macerated		
Agave salmiana Otto ex Salm-Dyck	Maguey	Agavaceae	Steam macerated		
Ageratina petiolaris Moc. & Sessé ex DC.	Hierba del ángel o Yolochichotl	Asteraceae	Plant (aerial) infusion		Terpens
Ageratum conyzoides L.	Hierba dulce	Asteraceae	Plant (aerial) infusion		Flavonoids, essential oils, terpens
Allionia choisyi Standl.	Hierba de la hormiga	Nyctaginaceae	Plant (aerial) infusion		
Allium cepa L.	Cebolla	Liliaceae	Bulbs raw		Sulfuric compounds
Alloispermum integrifolium (DC.) H. Rob.	Prodijiosa	Asteraceae	Plant (aerial) infusion		
Aloe barbadensis Mill.	Sábila	Liliaceae	Steam roasted, juice of the leaves	Normal rabbits (−)	Polysaccharides, flavonoids
Aloe vera (L.) Burm. F	Sábila	Liliaceae	Mixed with Nopal taken orally before meals	Normal mice (+)	Polysaccharides A B, flavonoids, terpens
Ambrosia artemisiifolia L.	Artemisa	Asteraceae	Plant (aerial) infusion		Sesquiterpen lactones
Anacardium occidentale L.	Marañon	Anacardiaceae	Bark infusion		
Ananas comosus (L.) Merr.	Piña	Bromeliaceae	Juice of the fruit		Monoterpenoids, Carotenoids, Lactones
Annona cherimola Mill.	Chirimoya	Annonaceae	Bark infusion		Isoquinolin Alkaloids
Annona glabra L.	Anona silvestre, palo de corcho	Annonaceae	Juice of the fruit root infusion		Diterpens, Alkaloids
Annona muricata L.	Guanabana	Annonaceae	Fruit raw		
Apodanthera buraeavi Cogn.	Pisto	Cucurbitaceae	Plant (aerial) infusion		
Aporocactus flagelliformis (L.) Lem.	Flor de junco	Cactaceae	Flowers infusion, steam infusion		
Arachis hypogaea L.	Cacahuate	Fabaceae	Seeds and oil		Sterols, flavonoids
Arceuthobium vaginatum (Humb. & Bonpl. ex Willd.) J. Presl	Injerto	Loranthaceae	Plant infusion		
Arctostaphylos pungens Kunth	Pingüica	Ericaceae	Leaves infusion, roots infusion		Tannins
Argemone mexicana L.	Chicalote, Cardo lechero.	Papaveraceae	Plant (aerial) infusion		Alkaloids, flavonoids
Argemone ochroleuca Sweet	Chicalote	Papaveraceae	Plant (aerial) infusion		Alkaloids
Argemone platyceras Link & Otto	Chicalote	Papaveraceae	Plant (aerial) infusion		
Aristolochia asclepiadifolia Brandegee	Guaco	Aristolochiaceae	Plant infusion EtOH		
Aristolochia malacophylla Standl.	Guaco	Aristolochiaceae	Flowers infusion		
Aristolochia sericea Benth.	Guaco	Aristolochiaceae	Steam infusion		

Table 1 (*Continued*)

Scientific name	Common name	Family	Plant part used and preparation	Pharmacological STudies*	Phytochemical informat**
Artemisia absinthium L.	Ajenjo	Asteraceae	Leaf boil		Sesquiterpen lactones, flavonoids
Artemisia ludoviciana Nutt.	Estafiate	Asteraceae	Plant (aerial) infusion		
Artemisia vulgaris L.	Ajenjo	Asteraceae	Leaf boil		Sesquiterpens flavonoids
Asclepias linaria Cav.	Romerillo	Asclepiadaceae	Plant (aerial) infusion		Sterols, triterpenoids
Barosma betulina Bartl. & H.L. Wendl.	Buchü	Rutaceae	Leaves infusion		
Bauhinia divaricata L.	Pata de vaca	Fabaceae	Leaf boil, flowers boil	Normal rabbits (+)	
Begonia heracleifolia Schltdl. & Cham.	Mano de león	Begoniaceae	Steam infusion		
Berberis moranensis Schult. & Schult. f.	Palo muerto	Berberidaceae	Bark infusion		Cucurbitacines
Beta vulgaris L.	Betabel	Chenopodiceae	Juice of the leaves		Alkaloids, flavonoids
Bidens aurea (Aiton) Sherff	Té de milpa	Asteraceae	Plant (aerial) infusion		Essential oils
Bidens leucantha (L.) Willd.	Rosilla	Asteraceae	Plant (aerial) infusion	Alloxanic mice (++)	
Bidens odorata Cav.	Aceitilla, Mosote blanco	Asteraceae	Plant (aerial) infusion		Flavonoids, triterpens
Bidens pilosa L.	Aceitilla	Asteraceae	Plant (aerial) infusion	Alloxanic mice (+)	Flavonoids, triterpens
Bocconia arborea S. Watson	Llora sangre	Papaveraceae	Leaves infusion		Alkaloids
Puemus boldus Molina J. A. Schultes & J. H. Schultes in J. J. Roemer & J. A. Schultes	Boldo	Monimiaceae	Plant (aerial) infusion		
Bouvardia ternifolia (Cav.) Schltdl.	Trompetilla	Rubiaceae	Leaves, steam infusion		Bouvardin
Brickellia cavanillesii (Cass.) A. Gray	Prodigiosa	Asteraceae	Plant (aerial) infusion	Normal rabbits (+)	Essential oils, brikelin
Brickellia squarrosa B.L. Rob. & Seaton	Amula	Asteraceae	Plant (aerial) infusion	Normal rabbits (+)	Flavonoids
Brosimum alicastrum Sw.	Ojite	Moraceae	Bark infusion		Benzoquinones
Buchnera pusilla Kunth	Chichibé	Scrophulariaceae	Bark infusion		
Buddleia stachyoides Cham. & Schltd/.	Hierba del perro	Loganiaceae	Leaves infusion		Flavonoids, alkaloids, essential oils
Buddleja Americana L.	Tepozán	Loganiaceae	Leaves infusion		Flavonoids, alkaloids
Buddleja cordata Kunth	Tepozán	Loganiaceae	Leaves infusion		Alkaloids
Bursera simaruba (L.) Sarg.	Cuajiote	Burseraceae	Bark infusion		Tannins
Byrsonima crassifolia (L.) Kunth	Nanche	Malpighiaceae	Fruit, bark infusion		Triterpenoids
Cacalia decomposita A. Gray	Matarique	Asteraceae	Root infusion	Alloxan Mice (++)	Alkaloids, polysaccharides
Cacalia peltata Kunth	Matarique	Asteraceae	Root infusion	Normal rabbits (++)	Polysaccharides
Calamintha macrostema Benth.	Tabaquillo	Lamiaceae	Root infusion	Alloxanic mice (+)	
Calea hypoleuca B.L. Rob. & Greenm.	Prodigiosa	Asteraceae	Plant (aerial) infusion		
Calea integrifolia (DC.) Hemsl.	Prodigiosa	Asteraceae	Stem, infusion		Sesquiterpen lactones
Calea zacatechichi Schltdl.	Prodigiosa	Asteracae	Leaves infusion	Normal rabbits (+)	
Calliandra anomala (Kunth) J.F. Macbr.	Cabello de ángel	Fabaceae	Leaves infusion		Triterpenoid saponins
Callicarpa acuminata Kunth	Xpuk'im	Verbenaceae	Root, infusion		
Capraria biflora L.	Sabadilla	Scrophulariaceae	Leaves infusion	Alloxanic mice (+)	Alkaloids, loiflorin
Carica papaya L.	Papaya	Caricaceae	Latex		Monoterpenoids
Carya Nutt.	Nogal	Juglandaceae	Leaves infusion		
Casimiroa edulis La Llave & Lex.	Zapote blanco	Rutaceae	Leaves infusion, bark infusion		Alkaloids, casimiroin, edulein, edulinin
Cassia fistula L	Caña Fístula	Fabaceae	Fruit		

Table 1 (*Continued*)

Scientific name	Common name	Family	Plant part used and preparation	Pharmacological STudies*	Phytochemical informat**
Cassia skinneri Benth.	Frijolillo	Fabaceae	Leaves infusion		
Cassia tomentosa L. f.	Retama cimarrona	Fabaceae	Leaves infusion		
Castela texana (T. & G.) Rose	Chaparro amargoso	Simaroubaceae	Bark infusion		Steroids
Castela tortuosa Liebm.	Venenilo	Simaroubaceae	Bark infusion		
Castilleja Mutis ex L. f.	Hierba del gato	Scrophulariaceae	Plant (aerial) infusion		
Catharanthus roseus (L.) G. Don	Vicaria	Apocinaceae	Root infusion		
Cecropia peltata L.	Guarambo	Cecropiaceae	Leaves infusion		
Ceiba pentandra (L.) Gaertn.	Ceiba, Pochote	Bombacaceae	Bark infusion		Essential oils
Centaurium brachycalyx Standl. & L.O. Williams	Tlanchalahua	Gentianaceae	Leaves infusion		
Centaurium calycosum (Buckley) Fernald	Tlanchalagua	Gentianaceae	Leaves infusion		
Chamaecrista hispidula (Vahl) H.S. Irwin & Barneby	Frijolillo	Fabaceae	Leaves infusion		
Chamaecrista hispidula (Vahl) H.S. Irwin & Barneby	Frijolillo	Fabaceae	Leaves infusion		
Chenopodium glaucum L.	Hierba del puerco	Chenopodiceae	Plant (aerial) infusion		
Chromolaena bigelovii (A. Gray) R.M. King & H. Rob	Ambula	Asteraceae	Plant (aerial) infusion		
Cirsium mexicanum DC.	Cardo santo	Asteraceae	Root infusion		
Cirsium rhaphilepis (Hemsl.) Petr.	Cardo santo	Asteraceae	Flower infusion		
Cissampelos pareira L.	Guaco	Menispermaceae	Root raw		Alkaloids, isoquinolin
Citrus aurantifolia (Christm.) Swingle	Limón	Rutaceae	Fruit		Essential oils, sesquiterpen lactones
Citrus limetta Risso	Lima	Rutaceae	Fruit		
Citrus sinensis (L.) Osbeck	Flor de azahar	Rutaceae	Ripe fruit infusion		Essential oils, flavonoids
Cnidoscolus aconitifolius (Mill.) I.M. Johnst.	Chaya	Euphorbiaceae	Leaves infusion		Polysaccharides
Cnidoscolus multilobus (Pax) I.M. Johnst.	Mala mujer	Euphorbiaceae	Leaves infusion		Triterpenoids, flavonoids, tannins
Cnidosculus chayamansa Mc Vaugh	Chayamansa	Euphorbiaceae	Leaves infusion		Flavonoids glycosides
Coix lacryma-jobi L.	Lágrima de San Pedro	Poaceae	Plant (aerial) infusion	Normal rabbits (+)	
Combretum farinosum Kunth	Bejuco de Carape	Combretaceae	Sap raw		
Conyza filaginoides (D C.) Hieron.	Simonillo	Asteraceae	Plant (aerial) infusion		Alkaloids, lenecin
Conyza gnaphalioides Kunth	Cimonillo, zacachichitl	Asteraceae	Leaves infusion		Terpens
Cordia elaeagnoides A. DC.	Cueramo	Boraginaceae	Bark infusion		Terpens
Cordia tinifolia Willd. Ex Roem. & Schult.	Palo mulato	Boraginaceae	Bark infusion		
Coriandrum sativum L.	Cilantro	Apiaceae	Plant (aerial) infusion		Coumarins, flavonoids, sesquiterpenoids, steroids
Costus mexicanus Liebm. ex Petersen	Caña de Jabalí	Zingiberaceae	Plant (aerial) infusion		
Costus rubber C. Wright ex Griseb.	Caña agria	Zingiberaceae	Plant (aerial) infusion		
Costus spicatus (Jacq.) Sw.	Caña de Jabalí	Zingiberaceae	Plant (aerial) infusion		
Crataegus mexicana Moc. & Sésse ex DC.	Tejocote	Rosaceae	Root infusion		
Crataegus pubescens (C. Presl) C. Presl	Tejocote	Rosaceae	Root infusion	Normal rabbits (++)	Tannins, flavonoids
Crotalaria acapulcensis Hook. & Arn.	Retama	Fabaceae	Leaves infusion		

Table 1 (*Continued*)

Scientific name	Common name	Family	Plant part used and preparation	Pharmacological STudies*	Phytochemical informat**
Croton draco Schltdl.	Sangre de Grado	Euphorbiaceae	Cortex infusion, latex		Diterpens
Croton torreyanus Müll Arg.	Salvia	Euphorbiaceae			
Cucurbita maxima Duchesne	Calabaza	Cucurbitaceae	Fruit juice		Sterols, flavonoids
Cucurbita mexicana Damm	Calabaza, Melón	Cucurbitaceae	Leaves infusion fruit juice	Normal rabbits (++)	
Cuscuta jalapensis Schltdl.	Sacapal	Convolvulaceae	Steam infusion		
Cyathea fulva (M. Martens & Galeotti) Fée	Árbol de la vida	Cyatheaceae	Root infusion		
Cyathea fulva (Martens & Galeotti) Fée.	Árbol de la vida	Filicaceae	Leaves infusion		
Cynara scolymus L.	Alcachofa	Asteraceae	Fruit infusion, flowers infusion		Flavonoids, sesquiterpen lactones, fenolic acids
Cynodon dactylon (L.) Pers.	Grama	Poaceae	Plant (aerial) infusion	Normal rabbits (+)	Flavonoids, terpens
Daucus carota L.	Zanahoria	Apiaceae	Root juice		Cumarines, flavonoids, essential oils, fenolic acids
Diospyros digyna Jacq.	Zapote negro	Ebenaceae	Fruit		
Dorstenia contrajerva L.	Contrayerba	Moraceae	Leaves bolied		Alkaloids, cardenolids
Dyssodia micropoides (DC.) Loes.	Hierba pelotazo	Asteraceae	Plant (aerial) infusion		
Elaphoglossum sp. Schott ex J. Sm.	Hierba del pastor	Lomariopsidaceae	Plant (aerial) infusion		
Equisetum giganteum L.	Limpia plata	Equisetaceae	Plant (aerial) infusion		Flavonoids
Equisetum hyemale L.	Cola de caballo	Equisetaceae	Plant (aerial) infusion		Flavonoids, alkaloids
Eriobotrya japonica (Thunb.) Lindll.	Níspero	Rosaceae	Leaves infusion, flowers infusion	Normal rabbits (−)	Sesquiterpens, flavonoids
Eucalyptus globules Labill	Eucalipto	Myrtaceae	Leaves infusion	Alloxanic mice (+)	Flavonoids, terpens
Euphorbia maculata L.	Hierba de la Golondrina	Euphorbiaceae	Leaves infusion		
Euphorbia prostrata Aiton	Hierba de la Golondrina	Euphorbiaceae	Leaves infusion		Flavonoids
Eysenhardtia polystachya (Ortega) Sarg.	Palo dulce	Fabaceae	Plant (aerial) infusion, bark infusion	Alloxanic mice (+)	Flavonoids, triterpens
Foeniculum vulgare Mill.	Hinojo	Apiaceae	Plant (aerial) infusion		Essential oils, flavonoids
Fouquieria splendens Engelm.	Albarda	Fouquieriaceae	Leaves infusion		
Fraxinus alba Marshall	Fresno	Oleaceae	Leaves infusion bark infusion		
Gnaphalium oxyphyllum DC.	Gordolobo	Asteraceae			Diterpens, flavonoids
Guaiacum coulteri A. Gray	Guayacan	Zygophyllaceae	Bark infusion		Alkaloids
Guaiacum sanctum L	Guayacan	Zygophyilaceae	Bark infusion		
Guardiola angustifolia (A. Gray ex S. Watson) B.L. Rob.	Chintuza	Asteraceae			
Guardiola tulocarpus A. Gray	Chintuza	Asteraceae	Leaves infusion		
Guazuma ulmifolia Lam.	Guázima	Sterculiaceae	Bark infusion		Alkaloids, tannins
Haemahtoxylon brasiletto H. Karst.	Palo Brazil	Fabaceae	Bark infusion		
Hamelia patens Jacq.	Balletilla	Rubiaceae	Leaves infusion		Tannins
Haplopappus venetus (Kunth) S.F. Blake	Xapulli	Asteraceae	Plant (aerial) infusion		
Hechtia melanocarpa L. B. Sm.	Maguey agrio	Bromeliaceae	Steam raw		Flavonoids, alkaloids
Heterotheca inuloides Cass.	Arnica	Asteraceae	Leaves infusion		Flavonoids, essential oils
Hibiscus rosa-sinensis L.	Tulipán	Malvaceae	Plant (aerial) infusion		Sterols, flavonoids
Hidalgoa ternata La Llave	Mozote de monte	Asteraceae	Plant (aerial) infusion		
Hintonia latiflora (Sesse & Moc. ex DC.) Bullock	Copalquin, Cáscara sagrada.	Rubiaceae	Bark infusion	Alloxanic mice (++)	Neoflavonoid, coutareagenin.

Table 1 (*Continued*)

Scientific name	Common name	Family	Plant part used and preparation	Pharmacological STudies*	Phytochemical informat**
Hippocratea excelsa Kunth	Cancerina	Hippocrateaceae	Root infusion		Sesquiterpens
Ipomoea starts Cav.	Tumba vaquero	Convolvulaceae	Plant (aerial) infusion		Essential oils
Jatropha dioica Cerv.	Sangre de grado	Euphorbiaceae	Root infusion		
Jatropha elbae J. Jiménez Ram.	Sangre de grado	Euphorbiaceae	Bark infusion		Terpens, flavonoids
Juliania adstringens (Schltdl.) Schltdl.	Cuachalalate	Julianiaceae	Bark infusion		Triterpens
Justicia spicigera Scheltdl	Muicle	Acanthaceae	Leaves infusion		Flavonoids
Kalanchoe pinnata (Lam.) Pers.	Tronador	Crassulaceae	Plant (aerial) infusion		Flavonoids
Karwinskia humboldtiana (Willd. ex Roem. & Schult.) Zucc.	Tullidora	Rhamnaceae	Leaves infusion		
Kohleria sp. Regel	Tlanchichinoli	Gesneriaceae	Leaves infusion		Triterpens
Larrea tridentata (Sessé & Moc. ex DC.) Coville	Gobernadora	Zygophylaceae	Plant (aerial) infusion		Terpens, lignans
Lepechinia caulescens (Ortega) Epling	Bretónica	Lamiaceae	Leaves infusion	Alloxanic mice (++)	Terpens
Lepidium virginicum L.	Lentejilla	Brassicaeae	Leaves infusion		
Leucaena leucocephala (Lam.) de Wit	Guaje	Fabaceae	Seed raw		Tannins
Leucophyllum texanum Benth.	Cenicillo	Scrophulariaceae	Plant (aerial) infusion		
Ligusticum porteri J.M. Coult. & Rose	Raíz de cochino	Apiaceae	Root infusion		Essential oils
Ligustrum japonicum Thunb.	Fresno	Oleaceae	Leaves infusion		
Loeselia coccinea (Cav.) G. Don	Hoja de la virgen	Polemoniaceae	Leaves infusion		Alkaloids, saponins
Loeselia mexicana (Lam.) Brand	Hierba de la virgen.	Polemoniaceae	Leaves infusion	Alloxanic mice (+)	Alkaloids, essential oils
Lonchocarpus cruentus Lundell	Guayacán	Fabaceae	Bark infusion		
Lopezia racemosa Cav.	Perilla	Onagraceae	Plant (aerial) infusion		
Lophocereus schottii (Engelm.) Britton & Rose	Muso	Cactaceae	Steam infusion		Alkaloids
Lysiloma acapulcense (Kunth.) Benth	Tepehuaje	Fabaceae	Leaves infusion, bark infusion		Tannins
Malmea depresa (Baillon) Fries	Elemuy	Anonaceae	Root infusion		Flavonoids
Malvastrum coromandelianum (L.) Garcke	Marvavisco	Malvaceae	Leaves infusion		Tannins
Mangifera indica L.	Mango	Anacardiaceae	Bark infusion leaves infusion		Flavonoids, essential oils, terpens
Marrubium vulgare L.	Marrubio	Lamiaceae	Leaves infusion, root infusion	Normal rabbits (++)	Terpens, flavonoids
Melothria pendula L.	Sandiita	Cucurbitaceae	Plant (aerial) infusion		
Mentha piperita L.	Hierbabuena	Lamiaceae	Leaves infusion		Essential oils, terpens, flavonoids
Mentha rotundifolia (L.) Huds.	Mostranza	Lamniaceae	Leaves infusion		Essential oils, terpens
Mentha suaveolens Ehrh.	Mastranzo	Lamiaceae	Leaves infusion		
Mimosa zygophylla Benth.	Gatuño	Fabaceae	Leaves infusion		
Mirabilis jalapa L.	Maravilla	Nyctaginaceae	Plant (aerial) infusion		Triterpens, flavonoids
Momordica charantia L.	Cundeamor,	Cucurbitaceae	Leaves infusion		Terpens, steroids, flavonoids
Morus nigra L.	Moral negro	Moraceae	Leaves infusion		
Musa sapientum L.	Flor de plátano	Musaceae	Root infusion		
Nasturtium officinale R. Br.	Berro	Brassicaeae	Plant (aerial) infusion		Flavonoids, alkaloids, terpens
Nopalea cochenillifera (L.) Salm-Dyck	Nopal	Cactaceae	Steam raw		

Table 1 (*Continued*)

Scientific name	Common name	Family	Plant part used and preparation	Pharmacological STudies*	Phytochemical informat**
Nopalea inaperta Schott ex Griffiths.	Nopal	Cactaceae	Steam raw		
Olea europaea L.	Hierba de oliva	Oleaceae	Leaves infusion		Alkaloids, flavonoids, terpens
Opuntia atropes Rose	Nopal bianco	Cactaceae	Steam raw		
Opuntia ficus-indica (L.) Mill.	Nopal	Cactaceae	Steam raw		Alkaloids, flavonoids
Opuntia fulgida Engelm.	Choya	Cactaceae	Steam raw		
Opuntia guilanchi Griffiths	Nopal blanco	Cactaceae	Steam raw		
Opuntia imbricata (Haw) DC.	Xoconostle	Cactaceae	Steam raw, fruit		
Opuntia leucotricha DC.	Duraznillo	Cactaceae	Steam		
Opuntia megacantha Salm-Dyck	Nopal blanco	Cactaceae	Steam raw		
Opuntia streptacantha Lem	Nopal	Cactaceae	Steam raw	Normal rabbits (+)	
Pachira aquatica Aubl.	Zapote de agua	Bombacaceae	Bark infusion		
Pachycereus marginatus (DC.) Britton & Rose	Organo, Sahuaro	Cactaceae	Steam raw		
Pachycereus pringlei (S. Watson) Britton & Rose	Cardón	Cactaceae	Steam raw		
Packera candidissima (Greene) W.A. Weber & Á. Löve	Lechugilla	Asteraceae	Plant (aerial) infusion		
Parathesis lenticellata Lundell	Chagalapoli	Myrsinaceae	Leaves infusion		
Parkinsonia aculeata L.	Bagote	Fabaceae	Leaves infusion		Flavonoids, triterpens
Parthenium hysterophorus L	Escobilla	Asteraceae	Plant (aerial) infusion		Alkaloids, partenin
Pavonia schiedeana Steud	Cadillo	Malvaceae	Leaves infusion	Normal rabbits (−)	Tannins
Persea americana Mill	Aguacate	Lauraceae	Leaves infusion		Sterols, flavonoids
Petroselinum crispum (Mill.) Nyman ex A.W. Hill	Perejil	Apiaceae	Plant (aerial) infusion		Essential oils, flavonoids
Phaseolus vulgaris L.	Fríjol	Fabaceae	Fruit infusion	Normal rabbits (+)	Essential oils, flavonoids, alkaloids
Phlebodium aureum (L.) J. Sm.	Calahuala	Polypodiaceae	Root infusion		Steroids
Phoradendron bolleanum (Seem.) Eichler	Injerto	Viscaceae	Plant (aerial) infusion		
Phoradendron tomentosum (DC.) Engelm. ex A. Gray	Muicle	Viscaceae	Plant (aerial) infusion		Phoratoxins
Phragmites australis (Cav.) Trin. ex Steud.	Carrizo	Poaceae	Plant (aerial) infusion		
Physalis coztomatl Dunal	Costomate	Solanaceae	Leaves infusion		
Physalis philadelphica Lam.	Tomate	Solanaceae	Fruit roasted	Normal rabbits (−)	
Piper auritum Kunth	Acoyo	Piperaceae	Leaves infusion		Terpens, flavonoids, essential oils
Piper hispidum Sw.	Cordoncillo	Piperaceae	Leaves infusion		
Piper sanctum (Miq.) Schltdl. ex C. DC.	Hierba Santa	Piperaceae	Leaves infusion		Essential oils, alkaloids
Piper schiedeanum Steud.	Tlaxalisnuat	Piperaceae	Leaves infusion		
Pithecellobium dulce (Roxb.) Benth.	Guamúchil	Fabaceae	Bark infusion		
Plantago australis Lam.	Gusanillo	Plantaginaceae	Plant (aerial) infusion		Lignans
Plantago major L.	Llante	Plantaginaceae	Plant infusion		Flavonoids, terpens
Plumbago scandens L.	Plumbago	Plumbaginaceae	w/i		Flavonoids
Plumeria rubra L.	Flor de mayo	Apocynaceae	Flowers infusion		
Polygonum acre Lam.	Sanguinaria	Polygonaceae	Leaves infusion		
Populus alba L.	Abedúl	Salicaceae	Leaves infusion		

Table 1 (*Continued*)

Scientific name	Common name	Family	Plant part used and preparation	Pharmacological STudies*	Phytochemical informat**
Porophyllum punctatum (Mill.) S.F. Blake	Piojillo	Asteraceae	Flowers infusion		
Portulaca denudata Poelln.	Verdolaga	Portulacaceae	Plant (aerial) infusion		
Portulaca oleracea L.	Verdolaga	Portulacaceae	Plant (aerial) infusion		Alkaloids, terpens
Pouteria hypoglauca (Standl.) Baehni	Baehni	Sapotaceae	Leaves infusion		
Prosopis juliflora (Sw.) DC.	Mezquite	Fabaceae	Fruit raw		
Prunus serotina subsp. capuli (Cav.) McVaugh	Capulín	Rosaceae	Fruit infusion		Terpens
Psacalium sinuatum (Cerv.) H. Rob. & Brettell	Matarique	Asteraceae	Root infusion		
Pseudosmodingium pemiciosum (Kunth) Engl.	Cuajilote	Anacardiaceae	Root infusion bark infusion		
Psidium guajava L.	Guayaba	Myrtaceae	Fruit		Terpens, flavonoids
Psidium yucatanense Lundell	Pach	Myrtaceae	Bark infusion		
Psittacanthus calyculatus (DC.) G. Don	Muérdago	Loranthaceae	Plant infusion, flowers infusion	Alloxanic mice (++)	
Quassia amara L.	Cuasia	Simaroubaceae	Leaves infusion		Alkaloids, terpens
Quercus acutifolia Neé	Encino	Fagaceae	Bark infusion		Terpens, flavonoids
Quercus rugosa Neé	Encino	Fagaceae	Bark infusion		
Randia echinocarpa Moc. & Sessé ex DC.	Grangel	Grangel	Leaves infusion		
Randia echinocarpa Moc. & Sessé ex DC.	Granjil	Rubiaceae	Fruit		
Raphanus sativus L.	Rábano	Brassicaceae	Root infusion		
Rhipsalis baccifera (J.S. Muell.) Steam	Niguilla	Cactaceae	Stem infusion, fruit raw		
Rhizophora mangle L.	Mangle	Rhizophoraceae	Bark infusion		Tannins
Ricinus communis L.	Huiguerilla	Euphorbiaceae	Leaves infusion		Flavonoids, terpens
Rosa centifolia L.	Rosa de castilla	Rosaceae	Leaves infusion		
Rubus adenotrichus Schltdl.	Zarzamora	Rosaceae	Leaves infusion		
Russelia equisetiformis Schltdl. & Cham.	Cola de caballo	Scrophulariaceae	Plant (aerial) infusion		
Salix taxifolia Kunth	Taray	Salicaceae	Steam infusion		
Salpianthus arenarius Humb. & Bonpl.	Catarinita	Nyctaginaceae.	Leaves infusion	Normal rabbits (++)	
Salvia leucantha Cav.	Salvia morada	Lamiaceae	Plant (aerial) infusion		Terpens
Samvitalia procumbens Lam.	Ojo de gallo	Asteraceae	Plant (aerial) infusion		Terpens
Saurauia pringlei Rose	Picon	Actnidaceae	Leaves infusion		
Sechium edule (Jacq.) Sw.	Chayote	Cucurbitaceae	Fruit raw		Flavonoids
Sedum dendroideum Moc. & Sessé ex DC.	Siempreviva	Crassulaceae	Plant (aerial) infusion		Sedoheoptulose
Sedum moranense HBK.	Siempreviva	Crassulaceae	Plant (aerial) infusion		
Sedum praealtum A. DC.	Siempreviva	Crassulaceae	Leaves infusion		
Selaginella lepidophylla (Hook. & Grev.) *Spring*	Doradilla	Selaginellaceae	Plant (aerial) infusion		Essential oils
Selaginella pallescens (C. Presl) Spring	Flor de piedra	Sellaginacae	Plant (aerial) infusion		
Selloa plantaginea Kunth	Diente de elef.ante	Asteraceae	Plant (aerial) infusion		
Senecio albo-lutescens Sch. Bip.	Matarique	Asteraceae	Root infusion		
Senecio palmeri A. Gray	Matarique	Asteraceae	Root infusion		
Senecio peltiferus Hemsl.	Matarique	Asteraceae	Root infusion		
Senna multiglandulosa (Jacq.) H.S. Irwin & Barneby	Retama china	Fabaceae	Leaves infusion		

Table 1 (*Continued*)

Scientific name	Common name	Family	Plant part used and preparation	Pharmacological STudies[*]	Phytochemical informat[**]
Senna obtusifolia L. (L.) H.S. Irwin & Barneby	Pa xojk	Fabaceae	Leaves infusion		Antraquinones, emodin
Senna occidentalis (L.) Link	Frijolillo	Fabaceae	Root infusion		Flavonoids, sterols
Serjania racemosa Schumach.	Bejuco tres en uno.	Sapindaceae	Plant (aerial) infusion		
Serjania triquetra Radlk.	Bejuco de tres C.	Salicaceae	Bark infusion		
Simira sp. Aubl	Quina roja, cáscara sagrada	Rubiaceae	Bark infusion		
Smilax aristolochiifolia Mill.	Zarzaparrilla	Similicaceae	Root infusion		Sapogenins
Solandra nitida Zuccagni	Flor de guayacán	Solanaceae	Flower infusion		
Solanum americanum Mill.	Hierba mora	Solanaceae	Plant (aerial) infusion		Alkaloids, solanin
Solanum brevistylum Wittm	Malabar	Solanaceae	Plant (aerial) infusion		
Solanum diversifolium Dunal	Malabar	Solanaceae	Leaves infusion	Normal rabbit (++)	
Solanum nigrescens M. Martens & Galeotti	Hierba mora	Solanaceae	Plant (aerial) infusion		
Solanum rostratum Dunal	Duraznillo	Solanaceae	Plant (aerial) infusion		
Solanum torvum Sw.	Berenjena	Solanaceae	Root infusion		
Solanum verbascifolium C.B. Wright	Berenjena	Solaneceae	Plant (aerial) infusion		Steroidal, alkaloids
Sonchus oleraceus L.	Lechuguilla	Asteraceae	Leaves infusion		Flavonoids
Spartium junceum L.	Retama	Fabaceae	Leaves infusion		
Sphaeralcea angustifolia (Cav.) G. Don	Hierba del negro	Malvaceae	Plant (aerial) infusion		
Stachytarpheta jamaicensis (L.) *Vahl*	Verbena	Verbenaceae	Plant (aerial) infusion		Terpens
Stenocereus marginatus (DC.) Berger & Buxb	Organo de Zopilote	Cactaceae	Steam roasted		
Struthanthus densiflorus (Benth.) Standl.	Injerto	Loranthaceae	Leaves infusion		
Swietenia humilis Zucc.	Zopilote	Meliaceae.	Seed raw		
Tagetes erecta L.	Cempasuchil o Flor de muerto,	Asteraceae	Plant (aerial) infusion		Terpens, essential oils
Tamarindus indica L.	Tamarindo	Fabaceae	Pulp of fruit raw		Flavonoids
Taraxacum qfficinale Weber ex F.H. Wigg.	Diente de león	Asteraceae	Leaves infusion		Terpens
Taxodium mucronatum Ten.	Ahuehuete	Taxodiaceae	Leaves infusion		Flavonoids
Tecoma starts (L.) Juss. ex Kunth	Tronadora	Bignoniaceae	Leaves infusion, plant infusion plant infusion	Alloxanic mice (++) Normal Dogs (++)	Alkaloids, terpens
Terminalia catappa L.	Castaño	Combretaceae	Fuit		
Teucrium cubense Jacq.	Agrimonia	Lamiaceae	Leaves infusion	Normal rabbits (+)	
Thriallis glauca (Cav.) Kuntze	Amargoso	Malphigiaceae	Root infusion		Flavonoids, terpens
Tillandsia usneoides (L.) L.	Heno	Bromeliaceae	Plant (aerial) infusion	Alloxanic mice (++)	Flavonoids
Tournefortia hirsutissima L.	Lagrima de San Pedro.	Boraginaceae	Steam infusion		
Tournefortia petiolaris DC.	Lagrima de San Pedro.	Boraginaceae	Steam infusion		
Tradescantia pendula (*Schnizl*.) D.R. Hunt	Comellina	Commelinaceae	Leaves infusion		Flavonoids
Trigonella foenum-graecum L.	Fenogreco	Fabaceae	w/i		
Tropaeolum majus L.	Mastuerzo	Tropaeoleaceae	Leaves infusion		
Turnera diffusa Willd ex Schult.	Damiana.	Turneraceae	Leaves infusion		Flavonoids, terpens
Urtica dioica L.	Ortiga	Urticaceae	Plant (aerial) infusion	Normal rabbits (−)	Flavonoids, coumarins
Urtica mexicana Liebm.	Ortiga	Urticaceae	Leaves infusion		

Table 1 (*Continued*)

Scientific name	Common name	Family	Plant part used and preparation	Pharmacological STudies*	Phytochemical informat**
Valeriana edulis Nutt. ex Torr. & A. Gray	Valeriana	Valerianaceae	Root infusion		
Valeriana procera Kunth	Valeriana	Valerianaceae	Root infusion	Alloxanic mice (−)	
Verbesina crocata (Cav.) Less.	Capitaneja	Asteraceae	Leaves infusion	Alloxanic mice (+)	
Verbesina persicifolia DC.	Huichin	Asteraceae	Plant (aerial) infusion	Alloxanic mice (+)	Sesquiterpens
Zaluzania angusta (Lag.) Sch. Bip.	Limpia tuna	Asteraceae	Root infusion		
Zantoxylum fagara L.	Tankasché	Rutaceae	Leaves infusion		Alkaloids
Zea mays h.	Pelos de elote	Poaceae	Fruit infusion		
Zexmenia gnaphalioides A. Gray	Peonia	Asteraceae	Root infusion		
Zizyphus acuminate Benth	Corongoro, amol	Rhamnaceae	Plant (aerial) infusion		

* In the Animal studies +, indicates activity and the level of it, while—mean no observed activity for the tested extract.
** The phytochemical information, refers about the reports for the plant no the active compounds.

isolated from *Psacalium* spp., processes for obtaining the novel eremophilanolide sesquiterpenes and methods for their use as hypoglycemic agents, for example, in the treatment of diabetes." Sadly, Mexicans have had no say in developing this patent on a Mexican plant.

Instead we review the current information of some lesser known plants commonly used in México to treat type 2 diabetes and summarise and discuss ethnobotanical, pharmacognostical, phytochemical, pharmacological and clinical data for the main species reported as hypoglycaemic in México (Table 1).

3. Ethnopharmacology of commonly used antidiabetic plants in México

Seven species used throughout México, reported in the international literature with pharmacological and phytochemical studies are discussed in greater detail and their potential for developing phytomedicines with a validated profile of activity and demonstrated safety profile is analysed (Table 2).

3.1. *Cecropia obtusifolia Bertol. (Cecropiaceae)*

The hypoglycaemic effect of this plant sold on several markets as a treatment for type 2 diabetes is well known in México, DF (Andrade-Cetto, 1999) and it is also known from many ethnobotanical collections in rural lowland areas (e.g. Heinrich, 1989).

3.1.1. *Botanical description*

A monopodic tree 20 m tall, growing in secondary vegetation in the tropical rain forest. This tree has a tall, straight, hollow trunk and a stratified treetop with few large branches growing horizontally from the trunk. The leaves are in a spiral disposition located at the top of the branches and are simple, peltate or deeply palmate, with a deep green colour in the upper face and grey at the lower surface. It is a fast-growing pioneer tree from tropical America, the hollow septate twigs are inhabited by ants (Pennington and Sarukhán, 1998).

3.1.2. *Distribution*

It is widespread in México, along both coasts, from Tamaulipas and San Luis Potosi to Tabasco on the Gulf of México, and from Sinaloa to Chiapas on the Pacific side. It is, in fact, a weedy species, which would presumably be relatively easy to grow on a larger scale or to harvest it sustainably by collecting material in the first few years after a *milpa* (corn field) has been given up.

3.1.3. *Ethnobotany*

Traditionally the dry leaves (15 g) are boiled in water (500 ml), the resulting infusion is cooled in the pot, then filtrated and drunk as "agua de uso". The cold infusion is consumed over the day or when the people have thirst. The use is reported from the following Mexican states, Hidalgo, Guerrero, Veracruz, Yucatan, Campeche, Tabasco, Edo. de México, Oaxaca and Chiapas. The traditional names include "Guarumbo", "Chancarro", "Hormiguillo", "Chiflon" and "Koochlé" among others.

3.1.4. *Main constituents*

The following constituents have been reported: β-sitosterol, stigmasterol, 4-ethyl-5-(*n*-3valeroil)-6-hexahydrocoumarin and 1-(2-methyl-1-nonen-8-il)-aziridine (Argueta, 1994). The type of extract for the isolated compounds has not been specified. From the butanolic extract Andrade-Cetto and Wiedenfeld (2001) isolated chlorogenic acid and isoorientin (Fig. 1 compounds **1** and **2**). The isolated compounds are also found in the medicinal tea.

3.1.5. *Pharmacology*

A hypoglycaemic effect of the water extract was demonstrated in alloxan diabetic mice (Pérez et al., 1984), in hyperglycaemic rabbits (Román-Ramos et al., 1991) and in

Table 2
Overview on antidiabetic effects of the seven species reviewed and commonly used in México (for references see text)

Botanical species	*Cecropia obtusifolia*	*Equisetum myriochaetum*	*Acosmium panamense*	*Cucurbita ficifolia*	*Agarista mexicana*	*Brickellia veronicaefolia*	*Parmentiera aculeata*
Animal model	Streptozotocin diabetic rats.	Streptozotocin diabetic rats	Streptozotocin diabetic rats	Hyperglycaemic rabbits Alloxan mice and rats	Normal and alloxan mice and rats	Normal and alloxan mice	Normal and alloxan mice
Clinical studies	In progress	In humans, positive	None	In humans, positive	None	None	None
Bioactive compounds	Chlorogenic acid (1), isoorientin (2)	Kaempferol-3-*O*-sophoroside, kaempferol-3,7-di-*O*-β-glucoside, caffeoyl-methylate-4-β-glucopuranoside kaempferol-3-*O*-sophoroside-4′-*O*-β-glucoside (3)	Caffeic acid desmethyl yangonine its $O^{4'}$-mono and di(1–6) glucoside (4 and 5)	Unknown	12-ursene 23,24 dimethyl 1-24-ethyl-sigmast-25-ene (6 and 7)	5,7,3′-trihydroxy-3,6,4′-trimethoxy flavone (8)	Lactucin-8-*O*-methylacrylate

Streptozotocin diabetic rats (Andrade-Cetto et al., 2000). Pérez-Guerrero et al. (2001) performed several pharmacological tests in male Swiss albino mice and concluded that the water extract of the leaves has low toxicity, a substantial effect as a central depressor, anti-inflammatory and analgesic effects. The report of Pérez et al. (1984) shows activity after 5 h of intraperitonal and oral administration of the aqueous extract (obtained from 50 g leaves boiled in 250 ml distilled water). This study does not give more details about the effects between time 0 and 5 h. Also, a proper positive control like glibenclamide is missing. There is no statistical evaluation of the data and the dose administered to each animal is not mentioned. The study by Román-Ramos et al. (1991) does not use a proper diabetic animal model (Versphol, 2002). Instead, it was conducted in healthy rabbits obtaining a glucose tolerance curve. The effect of the aqueous extract of 132 g leaves boiled in 1 l water and administering the infusion (4 ml/kg) using a gastric tube showed a significant hypoglycaemic effect at 60 min after the administration of the extract, and showed no activity after 4 and 5 h. Since the amount of dry extract administered was not measured in either study, the actual doses are missing. Also, in the study performed by Pérez et al. the reported activity is after 300 min (5 h) and Roman-Ramos et al. report no activity at this time.

In the study by Andrade-Cetto and Wiedenfeld (2001) in Streptozotocin diabetic rats, a positive and an untreated control was used, the water and butanolic extracts as well as the isolated compounds were tested, the hypoglycaemic effect is observed from 60 to 180 min for all the tested samples, with statistical significance. However, according to Versphol (2002) the animal model resembles more type I diabetes than type 2, while Islas-Andrade et al. (2000) provided evidence that using this model in a proper way diabetes type 2 can be mimicked.

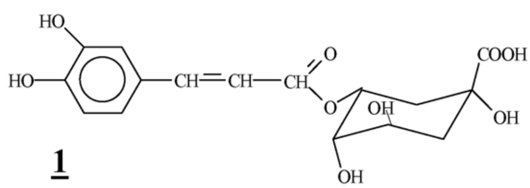
Herrera-Arellano et al. (2004) performed a study on diabetic type 2 people, they conclude that the plant has a significant hypoglicemic effect after 21 days of oral administration, of 3 g/day of the plant. The Cecropia group was also treated with glibenclamide at different doses, and no proper controls were used, so there is no point of comparison, and the effect can not be only attributed to the extract. The authors argue that the plant was given in a similar way as the traditional preparation, but the traditional preparation takes between 12 and 15 g plant/day.

3.1.6. Possible mechanism of action

Chlorogenic acid was identified as a specific inhibitor of the glucose-6-phosphate translocase component (Gl-6-P translocase) in microsomes of rat liver (Hemmerle et al., 1997). Simultaneous targeting of gluconeogenesis and glycogenolysis with an inhibitor of Gl-6-P translocase would result in a reduction of hepatic glucose production. The action of chlorogenic acid may well explain the hypoglycaemic effect observed by Pérez et al. (1984). The hypoglycaemic effect observed in mice after 5 h of experiment may be due to a lack of hepatic glucose production resulting in a hypoglycaemic state. This would have been caused by the liver not providing glucose due to the action of cholorogenic acid during the fasting of the animals. In the work by Román-Ramos et al. (1991), the animals were not fasted and they received an oral glucose charge at times 0 and 60 min at a dose of 2 g/kg. The authors did not observe any hypoglycaemic effect after 5 h, they argued that with this animal model glycaemia reaches basic values within 300 min. If the basic glycaemic value is reached at 300 min then the hepatic production of glucose has not been trigger, and there was no hypoglycaemic effect observed, and of course, no action of the cholorogenic acid.

The other compound isolated by Andrade-Cetto and Wiedenfeld (2001), isoorientin, had previously been tested by Afifi et al. (1999). They showed that the compound caused concentration-dependent inhibition of the amplitude and frequency of the phasic contractions of the rat and guinea-pig uterus but did not affect the isolated aorta, ileum or trachea. Deliorman-Orhan et al. (2003) tested the hepatoprotective activity of *Gentiana olivieri* and conclude that the effect "might possibly [be] due to the potent antioxidant activity of isoorientin". The antioxidant effect of plants used in diabetes treatment was shown by Letitia et al., 2002. According to these authors, the benefits of antioxidants in the prevention of the complications of diabetes supports and validates the use of the traditional medicine. Antioxidants are important in preventing diabetes, with low levels of plasma antioxidants implicated as a risk factor for the development of the disease,

Cecropia obtusifolia



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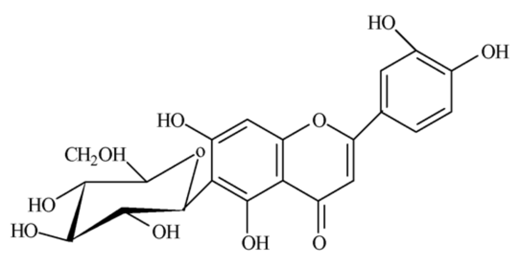

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Equisetum myriochaetum

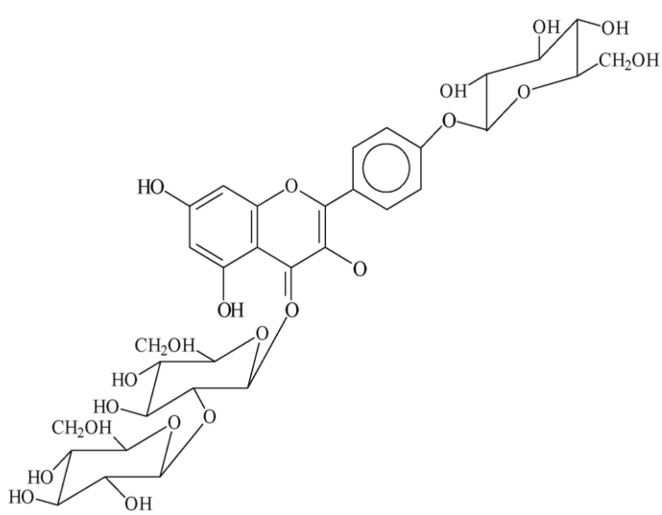

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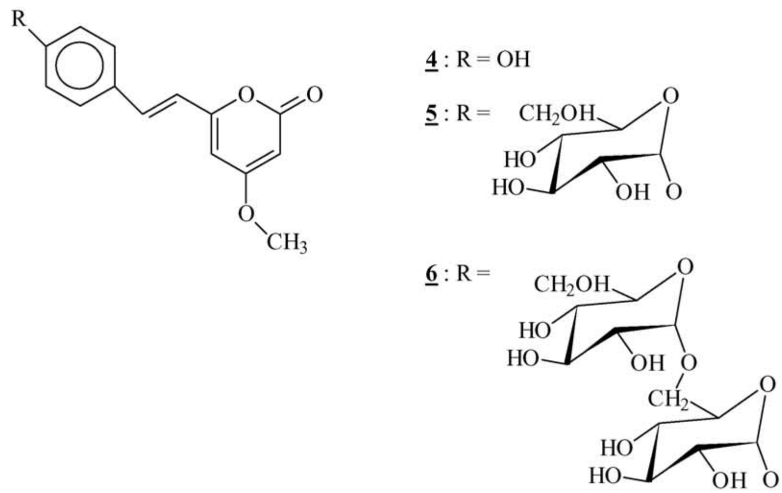
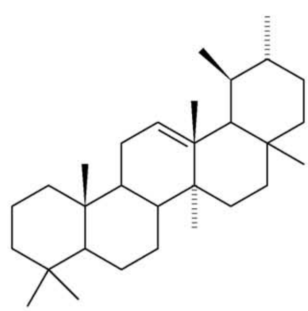
Fig. 1. Natural products with documented hypoglycaemic effects from the species discussed in detail in this review.

Acosmium panamense



Agarista mexicana



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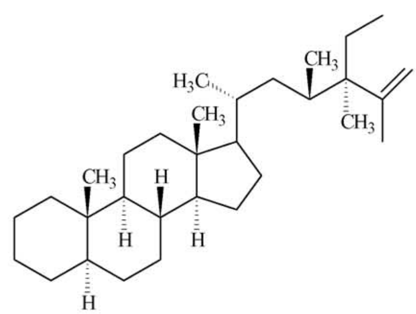

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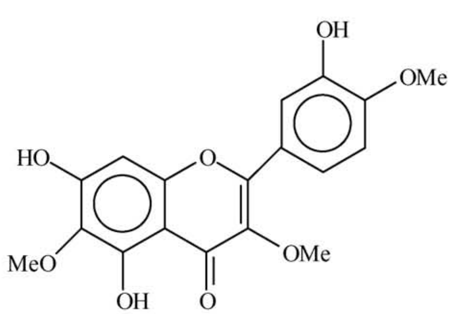
Brickellia veronicaefolia



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Arocomia mexicana

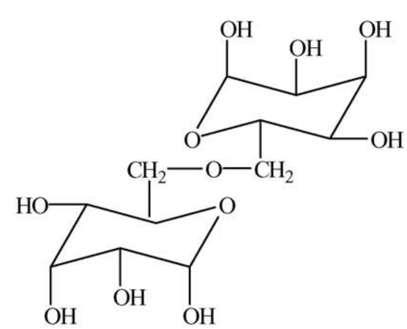

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Fig. 1. (*Continued*).

while throughout the progression of diabetes high levels of circulating radical scavengers have been recorded (Letitia et al., 2002).

Many of the complications of diabetes, including retinopathy and atherosclerotic vascular disease, the leading cause of mortality in diabetics, have been linked to oxidative stress (Baynes, 1991). In diabetic patients, isoorientin decreases the circulating of radical scavengers, and reduces symptoms of associated complications. However, the hypoglycaemic effect of this compound has not yet been tested.

3.1.7. Toxicity

In the previously mentioned work by Pérez-Gutiérrez et al. (2001) the acute toxicity was tested in Swiss mice. The authors conclude: “the median lethal dose (LD_{50}) of aqueous extract from *Cecropia obtusifolia* after i.p. administration is 1450 mg/kg animal (11.21 g of plant/kg of weight)”. This is the equivalent to 673 g for a 60 kg person, far higher than the commonly used dose of 15 g per person and day. The authors conclude that the aqueous extract of the plant has low toxicity.

3.1.8. Cecropia obtusifolia—conclusion

Some evidence mostly from *in vivo* animal studies is available which validate the use of *Cecropia obtusifolia* in diabetes. More studies are needed on type 2 diabetic animals and in patients to elucidate the complete hypoglycaemic mechanism of *Cecropia* extract. The extract has two main bioactive compounds, chlorogenic acid may well be responsible in part for the observed effect—the strongly reduced glucose production by the liver in a fasting state. However, since Andrade-Cetto and Wiedenfeld (2001) and Román-Ramos et al. (1991) reported an early hypoglycaemic effect, this action cannot be due to chlorogenic acid. Furthermore studies focusing on chronic application over longer time periods (at least one or two months) may also help to elucidate the mechanism of action. In such a study, data on the insulin production should be recorded, too. An extract from this species has a great potential to be further developed into a phytomedicine to treat type 2 diabetes in humans.

3.2. Equisetum myriochaetum Schlecht & Cham (Equisetaceae)

The plant is sold in several markets in México to treat kidney diseases (mal de orin) and diabetes.

3.2.1. Botanical description

Terrestrial plant with aerial stems 2–5 m (to 8 m) high, branched with regular verticilies 2–23 mm in diameter with 16–48 channels, terminal strobile in the branches and in the main stem 10 mm long and 4 mm in diameter (Palacios-Rios, 1999).

3.2.2. Distribution

It is known from the following Mexican states: Nayarit, Michoacán, Guerrero, Nuevo Leon, San Luis Potosí, Tamaulipas, Hidalgo, Puebla, México, Veracruz, Oaxaca and Chiapas. Again, it is a weedy species and there seems to be ample opportunity for collecting material form this species in a sustainable way.

3.2.3. Ethnobotany

Species of equisetum, mainly *Equisetum hymale*, *Equisetum laevigatum* and *Equisetum myriochaetum*, are traditionally used against kidney diseases. They are sold indistinctly on the markets. Traditionally, a decoction of the aerial part of the plant is prepared and consumed as “Agua de uso” (Argueta, 1994) The use as treatment of type 2 diabetes was described by Andrade-Cetto et al. (2000), the form of preparation is the same as for *Cecropia obtusifolia*.

3.2.4. Main constituents

From the butanolic and the water extracts with hypoglycaemic activity the following constituents were isolated: kaempferol-3-*O*-sophoroside, kaempferol-3,7-di-*O*-β-glucoside, caffeoyl-methylate-4-β-glucopuranoside and kaempferol-3-*O*-sophoroside-4ǐ-*O*-β-glucoside (Fig. 1, compound **3**, Wiedenfeld et al., 2000). Pinocembrin, chrysin, β-sitosterol, β-D-glycosyl-sitosterol, β-D-glucose and fatty acids were also mentioned as constituents of *Equisetum myriochaetum* (Camacho et al., 1992).

3.2.5. Pharmacology

The hypoglycaemic effect was demonstrated in Streptozotocin diabetic rats (Andrade-Cetto et al., 2000, and in diabetic type 2 patients (Revilla-Monsalve et al., 2002). Although the plant is reported mainly for kidney diseases it showed a remarkable hypoglycaemic effect in both tested models. There already exist reports about hypoglycaemic activities of various kaempferol derivatives containing plant extracts: Kaempferol 3-*O*-galactoside and Kaempferol 3-rhamnoglucoside from *Bauhinia variegata* (Andrade-Cetto, 1999), Kaempferol 3-*O*-rhamnoside from *Zizhyphus rugosa* (Khosa et al., 1983), Kaempferol 3-*O*-beta-glucopyranoside from *Morus insignis* (Basnet et al., 1993), and Kaempferol-3-*O*-(2gal-rhamnosilobonoside) from *Sterculia rupestris* (Desoky and Youssef, 1997).

A lower risk of type 2 diabetes has been associated with flavonoid intake specially quercetin and myrcetin (Knekt et al., 2002). The authors suggest an inverse association between flavonoid intake and subsequent occurrence of ischemic heart disease, cerebrovascular disease, lung and prostate cancer, type 2 diabetes, and asthma. The potential beneficial effect was associated with quercetin (the strongest antioxidant) but also with kaempferol.

The pharmacological testing in Streptozotocin diabetic rats showed a significant activity from 60 to 180 min, for the water and the butanolic extract. The most potent effect was shown by kaempferol-3-*O*-sophoroside-4′-*O*-β-glucoside. The water extract was also tested in type 2 diabetic patients. The results obtained in this study show a significant effect on the reduction of the glucose levels in these patients after the oral administration of an *Equisetum myriochaetum* water extract. The hypoglycaemic effect started 90 min after the administration of the decoction and was maintained for another 90 min. Insulin levels did not significantly change during the study, implying that the mechanism of action is not glibenclamide-like (not due to stimulation of insulin secretion).

3.2.6. Toxicity

In experiments performed with 200 male of *Drosophila melanoganster* (flr3/TM3,BdS), the traditionally used aqueous extract did not shown any toxicity, in up to 3700 ppm no LD_{50} was observed (Bárcenas-Rodríguez, 2004). The relevance of these data is, of course, limited.

3.2.7. Equisetum species—conclusion

The antioxidant effect of flavonoids cannot explain the acute effect of the plant. For developing a more widely used phytomedicine for use in type 2 diabetes, more studies are urgently required.

3.3. *Acosmium panamense (Benth.) Yacolev (Fabaceae)*

This species is widely used especially in the southern lowland of México for treating fever, malaria and in recent decades, diabetes (Heinrich, 1989).

3.3.1. Botanical description

Acosmium panamense (Benth.) Yacolev, (syn, *Sweetia panamensis* Benth, with traditional names "Guayacán" and "Bálsamo amarillo") is a tree up to 40 m height, growing in the tropical rain forest as a co-dominant species with *Terminalia amazonia* and *Vochysia guatemalensis* (Pennington and Sarukhán, 1998). The main characteristic of the tree is a tall, straight trunk pyramidal treetop with ascendant branches. The external cortex is plain and dark grey, the inner cortex is yellow and bitter. Leaves obtuse and pubescent surrounded by stipules with a spiral disposition. Fruit green to dark green legumes, 5–10 cm long (Pennington and Sarukhán, 1998).

3.3.2. Distribution

It grows along the Gulf coast from Veracruz to Yucatan and along the Pacific from Oaxaca to Chiapas. It is a co-dominant species from the tropical rain forest. It is often managed by local people (Heinrich, unpublished data), seems to be quite abundant, but no information on the potential of sustainable harvesting, especially if the bark is to be used, is available.

3.3.3. Ethnobotany

In Oaxaca the plant is used traditionally for the treatment of stomach pain, respiratory problems, diarrhoea, malaria and "marsh fever". The plant medicine is prepared as an infusion of the bark and it is taken orally 1–2 times per day. In addition, *Acosmium panamense* is utilized to treat diabetes in the village of Soteapan, Veracruz (Leonti et al., 2001; Leonti, 2002), and in Oaxaca (Andrade-Cetto and Wiedenfeld, 2004; Heinrich, 1989; Heinrich et al., 1992).

3.3.4. Main constituents

Phytochemical studies of the plant yielded several quinolizidine alkaloids like acosmine and acosminine, hydroxysparteine as well as lupinane alkaloids (Balandrin and Kinghorn, 1982; Argueta, 1994; Veitch et al., 1997; Nuzillard et al., 1999). From the water extract of the traditionally used bark (Wiedenfeld and Andrade-Cetto, 2003) caffeic acid and three pyrones were isolated: desmethylyangonine its $O^{4'}$-mono as well as the di(1–6)glucoside (Fig. 1, compounds **4**–**6**).

3.3.5. Pharmacology

The water and butanol extract as well as a mixture of the isolated substances (4 and 5) were tested in Streptozotocin diabetic rats. For all tested extracts the hypoglycaemic effect was statistically significant with respect to the control at 120 and 180 min. The main constituents of the traditionally used water extracts are the isolated pyrones, similar pyrones are found in *Piper methysticum* Forst. f. (Kava Kava) used until recently as (often licensed) phytomedicines for the treatment of anxiety disorders: 11-methoxy-5,6-dihydroyangonin, 11-methoxytetrahydroyangonin, tetrahydroyangonin, desmethoxyyangonin and yangonin, with the last two being the most abundant, (Ranjith et al., 2002). These compounds had previously not been evaluated for hypoglycaemic activity.

3.3.6. Acosmium panamense—conclusion

Limited *in vivo* evidence exists for the traditionally used water extract. The isolated pyrones have hypoglycaemic activity, but more studies are needed to clarify the mode of action.

3.4. *Cucurbita ficifolia Bouché (Cucurbitaceae)*

3.4.1. Botanical description

At the end of the 19th and the beginning of the 20th century, some authors were suggesting an Asiatic origin for *Cucurbita ficifolia*. Since the middle of the last century, the consensus has been that it is of American origin. However, its centre of origin and domestication are still unknown. Some authors have suggested Central America or southern México as places of origin, while others suggest South America, and more specifically the Andes (Purdue University, 2004).

Cucurbita ficifolia is a creeping or climbing plant, monoecious, annual, up to 10 m long. It is villose to softly pubescent with some short sharp spines dispersed over the vegetative parts. It has five vigorous, slightly angular stems and ovate-cordate to suborbicular-cordate leaves with 5–25 cm long petioles. The flowers are pentamerous, solitary, and axillary. The fruit is globose to ovoid-elliptical. The flesh is sweet and the seeds are ovate-elliptical, flattened, and of a dark brown to black or creamy white colour (Purdue University, 2004).

3.4.2. Ethnobotany

The popular name for the plant is "Chilacayote". The fruit, is used externally to treat a worm that runs under the skin (like *larva migrans*) in Hidalgo (Argueta, 1994). In México, the plants is consumed widely and several dishes and candies are prepared with the seeds or fruit. Aguilar et al. (1994) summarise the use of the fruit as a treatment of diabetes: the healers recommend the ingestion of the fruit macerated in water.

3.4.3. Main constituents

Lectins were isolated from stems and roots of 6-day old seedlings by precipitation with ethanol, affinity chromatography on Con A-Sepharose, gel filtration on Bio-gel P100 and separated by electrophoresis on polyacrylamide gel. Three purified lectins (RLA(1), RLA(2), RLA(3)) were obtained from roots and four from stems (SLA(1), SLA(2), SLA(3), SLA(4)) (Lorenc-Kubis et al., 2001). Acosta-Patino (2001) reports 90% of edible portion, 94% moisture, 0.3% fibre content, 1.2% protein, 17 mg calcium, 0.6 mg iron, 7 mg ascorbic acid, 0.03 mg thiamine, 100 g of *Cucurbita ficifolia* produces 3.34 Kjoule (14 Kcal). However, there is no report about the main constituents of the fruit extract.

3.4.4. *Pharmacology*

The pharmacological activity of the plant was tested in hyperglycaemic rabbits (Román-Ramos et al., 1991). The rabbits were submitted to glucose tolerance test and a preparation of the plant or tolbutamide was administrated, the animals receive 2 g/kg of glucose subcutaneously at the starting point and 60 min later. Water was used as control. The authors report a statistically significant hypoglycaemic effect of the plant from 60 min until 300 min. The amount of extract and the way of preparation are not reported in the paper.

Several experiments were performed by Alarcón-Aguilar et al. (2002) in alloxan induced mice and rats. Mature fruits of *Cucurbita ficifolia* were cut in halves. The juice was obtained with an electric extractor and freeze-dried. The acute effect was tested in *healthy* mice using two routes of administration, oral (po) and intraperitoneally (i.p.) at 500 mg/kg. In case of the po administration, the authors report an hypoglycaemic effect at 240 min with $p < 0.05$, while with the (i.p.) they observe statistically significant activity at 120 and 240 min. The acute effect was tested with the (i.p.) administration of the extract at 25, 250, 500, 594. 750, 1000, 1250 mg/kg, the hypoglycaemic effect was observed at 120 min with $p < 0.05$ for doses down to 750 mg and $p < 0.001$ for 1000 and 1250 mg at 240 min with $p < 0.001$ for all the doses, all compared with the control group. In alloxan diabetic mice, the acute effect was also tested at 500 mg/kg (i.p.), the authors report a hypoglycaemic effect with $p < 0.001$ at 120 and 240 min. Tolbutamide was used as control drug. The daily administration of 1000 mg/kg to alloxan diabetic rats, resulted in a gradual reduction of the blood sugar levels, at days 7 and 14, when the measures were taken.

In 2001, Acosta-Patiño tested the effect of the fruit juice in patients with moderate hyperglycaemia at 4 ml/kg (100 g of fruit = 75 ml of juice), Blood glucose levels were analyzed hourly during 5 h using a commercial enzymatic kit. In another session, at least separated by 8 days, the same group of patients received, the same amount of potable water as control. The authors report the hypoglycaemic effect at 180 min with $p < 0.05$, at 240 min with $p < 0.01$, and at 300 min with $p < 0.001$.

3.4.5. *Toxicity*

Some toxicity has been detected in the majority of the hypoglycaemic Cucurbitaceae species (Marles and Farnsworth, 1995) often due to cucurbitacines. The results from Alarcón-Aguilar (2002) showed that freeze-dried juice of *Cucurbita ficifolia* fruits had toxicity when administered intraperitoneally to mice and when it was orally administered daily for 14 days to alloxan-diabetic rats, the LD50 was 650 mg/kg with limits of 518.2 and 753. 8 mg/kg, while the administration of 1250 mg/kg cause the death of 100% of the animals.

3.4.6. *Cucurbita ficifolia—conclusion*

The fruit showed a hypoglycaemic activity in all the reported studies, the lack of phytochemical information on the juice (extract), prevents an assessment of the observed effect on a phytochemical level. In the clinical study, the authors conclude: “Due to the negligible content of fiber in *Cucurbita ficifolia* and the design of the study, the observed effects on glucose levels are not a consequence of glucose absorption changes in the intestine” (Acosta-Patino, 2001). In all cases, the doses used were high and the therapeutic relevance of this effects has to be questioned.

Extrapolating the toxicity levels reported in Alarcón-Aguilar (2002) to reach the lethal dose of 1250 mg/kg obtained from the freeze-dried juice, a person of 60 kg would need 75,000 mg (75 K) of fruit to have the lethal dose, and this is much higher than the traditionally recommended dose of 32 g. More studies are needed in order to identify the constituents of the fruits, and then test these substances. Quantitative phytochemical studies on the levels of lectins and other potentially relevant constituents during the development of the various organs of *Cucurbita ficifolia* and their link to potential toxic effects should also be conducted.

3.5. *Agarista mexicana (Hemsl.) Judd (Ericaeae)*

3.5.1. *Botanical description*

Shrub or tree to 8 to 11 m tall, with thick, corky, deeply furrowed bark; twigs very sparsely to densely pubescent, with nonchambered to clearly chambered pith; buds to ca. 1.5 mm long, leaves revolute. Inflorescences (fascicle-like) axillary racemes, flowers with triangular calyx lobes, with acuminate apices, capsules subglobose to short-ovoid (NYBG, 2004).

3.5.2. *Distribution*

Mountainous areas of México and Central America, from Veracruz and Jalisco south to Quintana Roo.

3.5.3. *Ethnobotany*

The water extract of the leaves of this plant known as “Palo Santo” is used orally to treat diabetes (Pérez-Guerrero et al., 2001).

3.5.4. *Main constituents*

From the chloroform extract of the dried steam of the plant, 12-ursene and the triterpene-23,24-dimethyl 1-24-ethyl-sigmast-25-ene were isolated (Fig. 1, compounds **7** and **8**).

3.5.5. *Pharmacology*

Blood glucose levels of normal and alloxan-treated diabetic mice and rats were determined after oral administration of the chloroform extracts of *Agarista mexicana* at 100 and 150 mg/kg. The oral administration of the extracts produced a significant hypoglycaemic effect in normal as well as in diabetic mice and rats (Pérez-Gutiérrez et al., 1996). The effect of the isolated compounds was tested in alloxan induced diabetic and in normoglycaemic mice at 50 mg/kg (i.p.). Compound **6** showed an statistically significant activity at 90 min, 180 min, 270 min and 1440 min (24 h), in alloxan diabetic mice, while the effect in normoglycaemic mice was observed at 90 and 270 min. Compound **7** shows statistically significant activity at 180 and 270 min in alloxan diabetic mice, and at 90 and 18 min in normoglycaemic mice, all this against the control groups. Tolbutamide was used as positive control (Pérez-Gutiérrez and Vargas, 2001).

3.5.6. *Agarista mexicana—conclusion*

The hypoglycaemic effect of the extract has been demonstrated and two terpenes were isolated as bioactive compounds, similar ursine triterpenes were isolated from the water-chloroform extract of the roots of *Tripterygium wildfordii* a traditional Chinese plant used against rheumatoid arthritis and other inflammatory and autoimmune disorders. However, the reported effect is of the total multi-glycoside extract, in which the ursenes are present together with other compounds (Duan et al., 2001). The therapeutic effect of the plant is attributed to the extract and not to a single compound. The mechanism of action of the isolated 12-ursene and the 23,24-dimethyl 1-24-ethyl-sigmast-25-ene is currently not known.

A comparison between the water extract (traditionally used) and the chloroform extract tested (e.g. regarding the presence of the bioactive compounds) would be of considerable interest. It is necessary to know the amount of bioactive compounds in the traditional tea, also toxicological testing is required in order to ensure the safety of the plant.

3.6. *Brickellia veronicaefolia (Kunth) A. Gray (Asteraceae)*

3.6.1. *Botanical description*

Bush 40 cm to 1 m tall, branched at the base with grey-red stems, white or pink flowers, present at the union of the stem and leaves.

3.6.2. *Ethnobotany*

The plant is know as "oregano de monte" the main use is against gall problems, especially bile, other uses are against stomach pain. For the later, the branch is boiled in water and a bitter infusion results (Argueta, 1994). The use against diabetes is reported in Pérez-Gutiérrez et al. (1998).

3.6.3. *Main constituents*

The following constituents have been isolated from the leaves: flavones – artementin, brickellin, casticin and trimetoxiquercetagenin, flavonols, eupatin, eupatolin, patuletin and vernicaefolin, and labdane diterpens (Argueta, 1994). From the chloroform extract Pérez et al. (2000) isolate the bioactive flavone 5,7,3′-trihydroxy-3,6,4′-trimethoxyflavone (Fig. 1, compound **9**).

3.6.4. *Pharmacology*

A chloroform extract of the leaves was tested in alloxan diabetic mice and normoglycaemic mice (i.p.) at 100, 200 and 300 mg/kg. The extract showed significant activity with at least $p < 0.01$ in both models for all the tested doses (at 90, 180, 270 and 1440 min = 24 h; Pérez-Gutiérrez et al., 1998). In the same models, the isolated flavone was tested (i.p. 10, 25 and 50 mg/kg). In the alloxan diabetic mice, 10 mg/kg shows statistically significant activity at 90, 270 and 1440 min with $p < 0.05$, 25 mg/kg shows statistically significant activity at 90 and 180 ($p < 0.01$) min, and at 270 and 1440 min ($p < 0.05$). 50 mg/kg shows activity only at 270 and 1440 min. In the normo-glycaemic mice, 10 mg/kg showed activity only at 270 min, 25 mg/kg was active at 90 and 180 min ($p < 0.01$) and at 1440 min ($p < 0.05$). 50 mg/kg showed activity at 90 and 180 min ($p < 0.01$) and at 1440 min ($p < 0.05$). In alloxan diabetic mice, the maximum effect observed was at 270 min, compared to the control groups. In all tests, tolbutamide was used as control.

3.6.5. *Brickellia veronicaefolia—conclusion*

The hypoglycaemic effect was confirmed and a bioactive compound has been isolated. The possible hypoglycaemic effect of flavonoids has been discussed above, there are no other reports of the isolated flavone. Toxicological test, as well as a comparative phytochemical investigation of the traditionally used and the tested chloroform extract would be highly desirable. The active doses reported by the authors are too high for use in traditional medicine or as a phytomedicine. In case of the chloroform extract, a person of normal weight (60 kg) would need 85 g of plant to get the desired effect.

3.7. *Parmentiera aculeata (Kunth) Seem. (Bignoniaceae)*

The fruit of the tree is reported to be hypoglycaemic, however the reports (Pérez-Gutiérrez et al., 1998, 2000a) discuss the species under a synonym: *Parmentiera edulis* DC.

3.7.1. *Botanical description*

Tree up to 15 m, branched since the base and channelled trunk, external cortex dark yellow with fissures and scaly ribs. The fruit is a berry up to 15 cm long by 6.5 cm wide, with several longitudinal furrows and a green-yellow colour.

The species is managed by humans to produce shade and is a widely distributed species known along the Gulf and Pacific coast from Tamaulipas to Yucatán and from Sinaloa to Chiapas (Pennington and Sarukhán, 1998).

3.7.2. *Ethnobotany*

The fruit and the cortex bark of the tree are boiled in water to treat kidney diseases, and for the treatment of diabetes

(Argueta, 1994). The plant is used in Guatemala to treat gonorrhoea (Caceres et al., 1995).

3.7.3. Main constituents

The guaianolide of lactucin-8-*O*-methylacrylate was isolated from the chloroform extract of the fruit. The hypoglycaemic activity was reportedly associated with this compound (Pérez et al., 2000). From the bark beta-sitosterol and tannins are reported (Argueta, 1994).

3.7.4. Pharmacology

The chloroform extract of the fruit was tested intraperitoneally in alloxan diabetic mice CD1 (strain) at 100, 200 and 300 mg/kg. For the dose of 100 mg/kg they report significant effects compared to the control at all observed times [90,270, 180 and 1440 (24 h) min]. For 200 mg/kg they also report effect at the same times, while the dose of 300 mg/kg shown also the same effects. However the different doses did not shown different effect.

Similar effects were observed in normoglucemic mice (Pérez-Gutiérrez et al., 1998c). Lactucin-8-*O*-methylacrylate isolated from the active fraction was tested (i.p.) on alloxan diabetic mice CD1. Again the data is reported as glucose reduction percent. At a dose of 10 mg/kg the authors report an significant hypoglycaemic activity at 90, 180 and 1440 min. Statistical significance was missed at 270 min. At a dose of 25 mg/kg significant activity is observed at 270 and 1440 min only, while at a dose of 50 mg/kg the activity is observed at 90, 180 and 270 min against the control group. Tolbutamide was used as reference (Pérez et al., 2000).

3.7.5. *Parmentiera aculeate*—conclusion

The hypoglycaemic effect of the chloroform extract and the isolated compound has demonstrated by the authors. However, the data (glucose values) of what happened between 270 and 1440 min is not reportedfor all the experiments. According to the data reported, the dose of 300 mg/kg of the fruit used in the first experiment, will be equivalent that a 60 kg person would have to eat 18 g of dried fruit for get the desired effect, which is to much for a single dose.

More studies are needed to know how the extract is working, in witch amount the isolated compound is present in the fruit, and as in previous examples there is no information on the bioavailability of the drug. Toxicity studies are also needed in order to develop a Phytomedicine.

3.8. Other species

As indicated in Table 1 many other species are commonly used in México. Some have received some attention in pharmacological and phytochemical studies.

Arocomia mexicana (Arecaecea), From the methanol extract of the root Pérez et al., 1997 isolated Coyolosa (Fig. 1, compound **9**) a tetrahydropyrane. The compound was tested on alloxan induced hyperglycemic mice and rats, at doses of 5.0–20 mg/kg i.p. the coyolosa exhibited significant blood sugar lowering at 1.5, 3.0, 4.5 and 24 h against the untreated control.

*Verbesina persicifoli*a DC. (Asteraceae; chloroform extracts at 100 mg/kg and 150 mg/kg) was tested in normal and alloxan diabetic mice. The authors conclude that those doses produced a significant hypoglycaemic effect in normal as well as in diabetic mice and rats (Pérez-Gutiérrez et al., 1996).

A hexane extract from *Cirsium pazcuarense* (Kunth) Spreng, (reported in the original paper as *Cirsium pascuarense*) at 100, 150 and 200 mg/kg i.p. showed a significant hypoglycaemic effect in normal as well as in diabetic mice. In addition, the extract altered glucose tolerance in alloxan induced diabetic rats. Chloroform and methanol extracts did not produce any significant change in blood glucose levels (Pérez et al., 2001). This is an example highlighting the need for proper taxonomic validation of a botanical identification.

The acute effects of the freeze-dried decoction of the roots of *Ibervillea sonorae* (S. Watson) Greene (Cucurbitaceae) on blood glucose levels were investigated in fasting mice. The authors report that: "the plant orally administrated to healthy mice did not cause a significant decrease of the blood glucose level. However, *Ibervillea sonorae* reduced the blood glucose of normal mice in a dose-dependent manner after intraperitoneal injection ($P < 0.05$). Also, this extract significantly lowered the glycaemia of mild alloxan-diabetic mice and rats, but did not in severe alloxan-diabetic rats, so it seems that this antidiabetic plant needs the presence of insulin to show its hypoglycaemic activity. Chemical, pharmacological, and toxicological investigations of *Ibervillea sonorae* must continue to establish its use as an alternative in the control of diabetes mellitus" (Alarcón-Aguilar et al., 2002).

Of note, at least three of the species discussed above are edible fruits. In Table 1, a large number of other food plants (most notably vegetables) are included: *Allium cepa* L. (Cebolla), *Ananas comosus* (L.) *Merr.* Piña), *Annona cherimola Mill.*, (Chirimoya), *Arachis hypogaea* L. (Cacahuate), *Asclepias linaria Cav*. (Romerillo), *Byrsonima crassifolia* (L.) *Kunth* (Nanche), *Carica papaya* L. (Papaya), *Casimiroa edulis* La Llave & Lex. (Zapote blanco), *Citrus aurantifolia* (*Christm*.) *Swingle* (Naranjo), *Citrus limetta* Risso (Lima), *Coriandrum sativum* L. (Cilantro), *Costus ruber* C. Wright ex Griseb. (Caña agria), *Crataegus pubescens* (C. Presl) C. Presl (Tecojote), *Cucurbita ficifolia* (L.) Bouché (Chilacayote), *Cucurbita mexicana Damm.* (Calabaza), *Cynara scolymus* L. (Alcachofa), *Daucus carota* L. (Zanahoria), *Eriobotrya japonica* (Thunb.) Lindll. (Níspero), *Leucaena leucocephala* (Lam.) *de Wit* (Guaje), *Nopalea cochenillifera* (L.) *Salm-Dyck* (*Nopal*), *Nopalea indica* L. (Nopal), *Persea americana Mill.* (Aguacate), *Petroselinum crispum* (Mill.), *Nyman ex A.W. Hill* (Perejil), *Phaseolus vulgaris* L. (Frijol), *Physalis philadelphica* Lamm (Tomate), *Piper auritum Kunth* (Hierba santa), *Portulaca oleraceae* L. (Verdolaga), *Psidium guajava* L. (Guayaba), *Sechium edule* (Jacq.) Sw. (Chayote), *Solanum verbascifolium Banks ex Dunal* (Berenjena), *Tamarindus indica* L. (Tamarindo). Phytochemically these are very diverse taxa, but the importance of such fruit certainly highlights the health beneficial effects of a diet rich in plant fibre. While currently specific pharmacological effects of this diverse group of species cannot be ascertained, it is possible that modification of the passage time or changes in the GI flora have an indirect influence. This opens a fascinating are of research at the interface of food and medicines (cf. Heinrich, 1998).

4. General conclusion

Clearly, a large number of species are used in today's México to treat diabetes or its symptoms. An interesting and unresolved issue relates to the way such uses were developed over the last decades. It seems that many of the species were originally used for a variety of kidney disorders and most notably for their diuretic effect. From an ethnopharmacological perspective, it would be extremely interesting to analyse this process further.

For further testing proper animal model have to be used (Versphol, 2002). Today, the models used resemble type 1 diabetes or are no models for diabetic testing like glucose overload. The only model with supporting data for type 2 diabetes is the Streptozotocin diabetic rat (Islas-Andrade et al., 2000). But according to Versphol (2002), the only way to get type 2 diabetic animals by chemical induction is by the proper use of Streptozotocin in neonatal rats (n-STZ), or use genetically models like fa/fa Zucker diabetic fatty rat. None of these models has been used until now to test Mexican plants, and according to the group of Pérez-Gutierrez et al. a method developed in 1964 is the most commonly used by them, so also there needs to be an update of the pharmacological tools we use.

We propose three levels of intervention led by the goal to reduce the public health impact of this syndrome involve government actions at all levels.

Nutritional education of the general population is a first step which could reduce the epidemic proportion of the disease. One core problem is the high consumption of sweet drinks commonly called "refrescos" all over México. When conducting field work in any region of México one cannot fail to note large quantities of discarded plastic bottles in each back yard. Also the consumption of such "referescos" is visible everywhere and at anytime. Therefore, strict regulations about the content of sugar in those drinks would be highly desirable (e.g. via a special sales tax), and of course it would be ideal to largely avoid such beverages. The government and health professionals should also promote exercise among people living in the cities, to avoid sedentary way of life.

Additionally, there must be some efforts to monitor and control the plants sold on markets and widely collected by the people for autoconsumption. Educational programmes together with pharmcodynamic studies should have first priority. The latter research should include projects on the species' mechanism of action, on the optimal doses and treatment schedule, and on the best mode of preparation. Even though pharmacoeconomic studies on the costs of such treatments are lacking, it is likely that, for example, cost of treatment with *Cecropia* leaves bought on the Mercado de Sonora in México, DF may easily reach MEX$ 250 (US$ 20) per month of treatment. This highlights another important point – the economic impact of using such herbal remedies has not been studied at all, but it is likely to be an important cost factor for many poorer families. The production of medicinal teas or simple preparations with ascertained quality that could be sold on markets should be promoted as part of this intervention. Such an approach would assure a health beneficial effect of the final product. We see efforts like this, for example on the market in Mérida, Yucatán (Andrade-Cetto., pers. obs.), where a healer is selling an ethanolic preparation of *Malmea depressa* (drops). As a next step simple quality control measures could be established. These initiatives must again be accompanied by the appropriate training and education programmes directed at diabetics, physicians and social workers to ensure that the people drink those preparations in a medically and pharmaceutically appropriate way. In order to achieve this we still have a long way to go and México with its rich tradition in medicinal plants use still lacks appropriate training for physicians and pharmacists in phytotherapy and phytopharmacy.

The third level on our opinion the most important one. It focuses on the development of a phytomedicine with hypoglycaemic effects at early stages of the disease or even prior to the start of the disease (during the period of increased insulin resistance). In this context, the isolation of the main compounds from the active extract is a crucial step in all R&D activities for developing a novel phytomedicine. The use of a phytomedicine is suggested because it would be subject to quality control, and could be prescribed by physicians. Herbal drugs are mainly whole, fragmented or cut, plants parts of plants, algae, fungi, lichen in an unprocessed state, usually in a dried form, but sometimes fresh. They are precisely defined by their botanical (scientific) binomial (Heinrich et al., 2004). The herbal drug preparation (phytomedicine) is obtained subjecting herbal drugs to treatments such as extraction, distillation, fractionation, purification, concentration and fermentation. These include cut or powered herbal drugs, tinctures, extracts, essential oils, fatty oils, expressed juices and processed exudates (Gaedcke and Steinhoff, 2003). Clearly, considerable research will be required for developing such products which could be of enormous benefit to the Mexican population suffering from a drastic increase in this chronic and debilitating disease. In comparing México with the examples of Germany or France, where the phytomedicine market moves billions of dollars each year, it becomes apparent that Mexican businessmen have an opportunity to develop such novel products. Alternatively, the Mexican Social Security System, which has for my years conducted research on popularly used medicinal plants, could take a lead and develop phytomedicines which would be available at relatively low cost.

A difficult and unresolved issue relates to the traditional intellectual property on these species. Clearly, they have been used widely in México, knowledge about these these species, their bioactive compounds and pharmacological effects is in the public domain, their use in the systematic treatment of diabetes is relatively recent and it will be nearly impossible to identify one group of people which can claim traditional ownership. However, since some of these phytomedicines may also be commercialised outside of México, the Mexican government or other appropriate institutions will have develop ways to guarantee the sustainable use of this species and that any economic benefit from these phytomedicines will also be shared with the Mexican people.

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