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Plants used in Mexican folk medicine with antidiabetic and antihypertensive properties

Edgar R. Esquivel-Gutiérrez, Ruth Noriega-Cisneros, Alfredo Saavedra-Molina, Rafael Salgado-Garciglia*
Instituto de Investigaciones Químico Biológicas, Universidad Michoacana de San Nicolás de Hidalgo, Edif. B3, Ciudad Universitaria 58030, Morelia, Michoacán, México
*rafael.salgadogarciglial@gmail.com

Abstract

Diabetes mellitus and hypertension (high blood pressure) are the most common diseases with high risk affecting most of the worldwide adult population in both sexes. In Mexico, cardiovascular diseases are the first cause of morbidity and mortality. Diabetes mellitus is the first cause of death in women and ischemic heart disease becomes the leading cause of mortality in men; high blood pressure is one of the major risk factors for coronary artery disease and stroke, is currently among the ten leading causes of death worldwide. Generally, for the therapeutic management of both diseases is using multiple drugs with different chemical structures and different mechanisms of action, which aim to normalize blood glucose and blood pressure levels. These are managed for a long time, which often represents a high economic cost. On the other hand, some patients have no adherence to treatment as this one, is ineffective, the adverse effects are situations that require change or discontinue medication immediately. With these remarks it is important the developments of new antidiabetic or antihypertensive agents, the medicinal plants are an option. Scientific interest aimed at the search phytotherapeutic drugs for the treatment of these diseases has led the conduct of research that validates the use of medicinal plants, or they have found new agents with antidiabetic and antihypertensive properties. In Mexico, has been reported at educational institutions and research, a number of plants widely used in Mexican folk medicine, with high potential to be used in the treatment of diabetes mellitus and hypertension.

KEY WORDS: MEDICINAL PLANTS, DIABETES MELLITUS, HYPERTENSION, ANTIDIABETIC, ANTIHYPERTENSIVE

Introduction

The ethnobotanical study is an important activity in the area of research and development of drugs since some reports claim that approximately 40% of pharmaceuticals consumed in developed countries come from natural sources, mainly from plants. In Mexico, most of the traditional knowledge that is about medicinal plants comes from pre-Hispanic times and different ethnic groups currently retain it. For more than 30 years has been the need to integrate traditional medicines within official systems to improve the quality of life of patients this for cultural and economic reasons (1).

The therapeutic effects of plants are due to the content of different secondary metabolites such as essential oils, tannins, phenolic acids, sesquiterpenlactones, ketones and flavonoids, among others (1). Among the plant secondary metabolites that are prescribed to patients that presents painful diseases and cancer, including taxol, active principle from *Taxus brevifolia* and *Taxus cuspidata*, a compound with anticancer activity (2); reserpine, synthesized by the species of *Rauwolfia serpentina* and *Rauwolfia vomitoria*, with antihypertensive activity and tranquilizer (3); and morphine and noscapine, the active compounds of *Papaver somniferum*, that are analgesic and antitumor, respectively (4, 5).

The main strategy developed to achieve the integration of folk medicines for disease treatments, has been the research in order to verify its effectiveness scientifically. In countries such as China, India and Thailand have been significant advances in the articulation of integrated models of health; while in some countries in Latin America like Mexico, Nicaragua and Brazil have interesting experiences with progress towards the integration of traditional medicines in modern medicine (6). Investigations in Mexico with medicinal plants have been developed from greatly in the last decade, indicative of the importance of the Mexican folk medicine.

Currently, the reports indicate the existence of scientific literature supporting the use of plants, extracts or their active compounds against various diseases such as diabetes, hypertension and cancer, or with antibacterial, antifungal, antiprotozoal, relaxing and sedative properties (1).

Diabetes mellitus and hypertension are two of the most important degenerative chronic diseases in Mexico, being the main cardiovascular risk factors, which tend to be frequently associated. Found that high blood pressure affects more than 20% of people in industrialized countries and diabetes is considered to be endocrine disease of higher incidence among the population (347 million worldwide) (6).

Diabetes and hypertension are not curable diseases, but with a control proper levels of glucose in the blood and in the normal values of blood pressure, can be avoided or help delay damages that occur in the body.

Both diabetes and high blood pressure are not curable diseases, however, with a control proper levels of blood glucose and in the normal values of blood pressure can be avoided or at least delay damage that occurs in the body (7). This can be achieved through changes in lifestyle (reduction of weight and physical exercise) or with pharmacological treatment.

Due to the high costs that may represent the treatment for both conditions, an alternative is the use of medicinal plants or active compounds derived from them, since they are considered safer and less expensive than allopathic, chemical synthesis-based treatments. The plants are an important source of biologically active substances, with great potential as drugs or as raw material for the pharmaceutical industry. The increase of the world population demand an increase of the sources of drugs, making it both developed and underdeveloped countries directed their efforts towards the evaluation and exploitation of the plants species, since the use of medicinal plants has increased as an alternative to the current health problems, especially in countries located in the tropics (8).

This paper describes some of the progress made in the last 12 years of scientific research conducted

in our country, using medicinal plants in order to demonstrate their effectiveness to diabetes and hypertension.

A history of the use of medicinal plants in Mexico

Mexico has a rich tradition in the use of medicinal plants among its several popular healing practices. The first book of Aztec medicinal herbs and one of the most important bibliographical historical sources in America in medicine, named "Book of the medicinal herbs of the Indians", it knew four centuries later as Badiano Codex (de la Cruz-Badiano Codex), it is a work that describes more than 150 Mexico native plants that have medicinal use (9).

It is estimated that Mexican medicinal flora contains between 3,000 and 5,000 plants that have therapeutic potential. A total of 3,000 species has been compiled in an atlas of medicinal plants used by various ethnic groups. Incredibly, approximately 1% of medicinal plants have been studied thoroughly in its medicinal properties. Therefore, it is clear that must be more clinical and ethnobotany research, to determine scientifically the medicinal benefit of these plants (1, 10).

Although the reports indicate a large number of medicinal plants used in our country, the most used are: cudweed (*Gnaphalium* sp.), blue gum *tree* (*Eucalyptus globulus*), peppermint (*Mentha* x *piperita*), chamomile (*Matricaria chamomilla*), indian fig (*Opuntia ficus-indica*), mexican arnica (*Heterotheca* sp.), trumpet tree or guarumo (*Cecropia obtusifolia*), vervain (*Verbena carolina*), yellow elder (*Tecoma stans*), epazote (*Chenopodium ambrosioides*), aloe vera (*Aloe vera*), rue (*Ruta graveolens*), rosemary (*Rosmarinus officinalis*), among others (11, 12).

Medicinal plants as a source of drugs

Currently, is the knowledge that many compounds derived from plants, whose pharmacological activity is important, are produced by additional metabolic pathways to primary metabolism, known as secondary metabolism by which these compounds are called secondary metabolites (13). Many of these metabolites, pure or mixtures possess various effects as stimulants, analgesics or therapeutic, are mostly used in the pharmaceutical, food and textile industries, in agrochemistry, perfumery and cosmetology (14).

The distribution of secondary metabolites in the plant Kingdom is very wide, it is estimated that about 50,000 plant species are used medicinally, of which only a 20% of them have been determined its medicinal properties (15).

Ethnobotanical knowledge is strongly linked to the cultural aspect and constitutes a particular indicator of population response to find cure for diseases. Recent works have reported that certain metabolites have pharmacological activity for the treatment of gastrointestinal, skin, central nervous system, cardiovascular diseases, cancer and diabetes, among other (16).

Diabetes and medicinal plants

Diabetes mellitus is a metabolic syndrome that is characterized by hyperglycemia, which is caused by defects in the secretion and action of insulin (17). Chronic hyperglycemia is associated with damage, dysfunction and failure of various organs. It especially affects eyes, kidneys, nerves, heart and blood vessels. The diabetic patient presents 40 times risk greater than their lower limb amputation, 25 times higher risk of end-stage renal failure, 20 times more than blindness, 2 to 5 times higher between 2 and 3 times greater of acute myocardial infarction and cerebrovascular accidents (18). It has also increased susceptibility of developing hypertension, dyslipidemia and obesity (19).

This disease constitutes a serious public health problem, it is estimated that currently 347 million people in the world suffer from it and approximately 35% of the diabetic population comes from industrialized countries and 65% of them live in developing countries (6). In Mexico, about 10% of the population has diabetes mellitus and it is estimated that the 90% cases are type II. It occurs most frequently in older adults and in obese people, so it has become the leading cause of death with 12% of the total deaths (20).

There are currently various medical strategies for diabetes control, one of them is research aimed at obtaining new hypoglycemic drugs that can help control the disease. However, in our country and in other underdeveloped countries, a sector of the population does not have access to modern treatment of this disease, due to the economic and cultural limitations. For this reason, herbal medicine or natural medicine provides the alternative with equal effectiveness but fewer side effects that occur with synthetic drugs, as well as being a cheaper therapy (21).

Medicinal plants or extracts thereof can optimize glucose metabolism and diabetes management not only by hypoglycemic effects but also to improve the lipid profile, antioxidant and capillary function. More than 400 products from plants are commercialized for the treatment of diabetes worldwide (22).

According to Marles and Farnsworth (23, 24), the botanical families that contribute with more species with antidiabetic properties around the world are Fabaceae, Asteraceae, Lamiaceae, Liliaceae, Poaceae and Euphorbiaceae, among others. Among the most important are Cucurbitaceae (*Momordica charantia*), Apocynaceae (*Catharanthus roseus*), Anacardiaceae (*Anacardium occidentale*), Liliaceae (*Allium cepa, Allium sativum* and *Aloe vera*), Myrtaceae (*Syzygium cumini*), Bignoniaceae (*Tecoma stans*), Urticaceae (*Urtica dioica*), and Fabaceae (*Lupinus albus* and *Trigonela foenum-graecum*). More recently, has been established the antidiabetic or hypoglycemic effect of Musaceae (*Musa paradisiaca*) (25), Malvaceae (*Guazuma ulmifolia*) (26) and a Fabaceae (*Deguelia rufescens*) (27).

Research with plants is usually conducted in laboratory animals with type I or type II diabetes induction. Most of these are performed at the experimental level, 90% are acute effect studies and only 10% of them are clinical and toxicological studies. In these, only 10% are with chronic treatments, many of them targeting the biological determination in the medium term (28).

Hypertension and medicinal plants

In the seventh report of the Committee of the Board national about the prevention, detection, evaluation, and treatment of high blood pressure (29), it is recommended to maintain values of arterial hypertension of < 140/90 mmHg for most patients and < 130/80 mmHg in patients with diabetes mellitus or kidney disease (30). High blood pressure affects approximately 26.4% of the adult population and between 60% and 70% people in the seventh decade of life (31). In Mexico, it is a disease very prevalent, because according to the national health and nutrition survey, for the year 2006 was presented at the 30.8% of the population older than 20, reporting that more than 50% of the men and 60% women over the age of 50 years they have it (32).

High blood pressure is a co-morbidity of extremely common in diabetics, affecting 20 to 60% of the population with diabetes mellitus. The prevalence of hypertension in diabetics is 1.5 to 3 times higher than in non-diabetics, so contributing to the development and progression of chronic disease complications. There is extensive epidemiological evidence that diabetics with high blood pressure have a higher risk of cardiovascular disease, kidney failure and diabetic retinopathy (33). In studies with patients with moderate systolic hypertension and impaired glucose tolerance in fasting (in non-diabetics), has been shown that these presenting increased risk of mortality from cardiovascular disease (34).

Pharmacological treatments with drugs are based on the control of hypertension by different mechanisms, as angiotensin-converting enzyme (ACE) inhibition, the use of type angiotensin receptor antagonists II (ARA II), thiazide type diuretics in low doses, calcium antagonists and â-blockers. In general, all of the available agents caused a reduction of about 10-15 mmHg in systolic blood pressure and 5-10 mm Hg in diastolic blood pressure (35).

Some of the plants with global importance antihypertensive activity are *Rauwolfia serpentina* (3), *Veratrum album* (36) and *Rhododendron molle*

(37). Ajmalicine, reserpine and rescinamamina are antihypertensive metabolites, isolated from *R. serpentina*; the protoveratrinas A and B are the active principles of *V. album*; and the romitoxina is the agent antihypertensive of *R. molle* (38).

Research in Mexico with antidiabetic and antihypertensive plants

Mexico has research centers and educational institutions such as the National Autonomous University of Mexico, the Autonomous University of the State of Mexico, the National Polytechnic Institute and others of the different states, which carry out research for the development of new herbal drugs. Through these works and an intensive program of drug tracking the selection of medicinal plants with therapeutic potential has been possible. Wild plants of our country, used in traditional medicine, have been evaluated to identify the major chemical components, to determine its pharmacological effects, the stability of its products and its clinical behavior, in order to find new compounds with medicinal properties or validate its folk medicinal use.

Some of these investigations have been conducted to evaluate the antidiabetic or antihypertensive effects of different plants growing in Mexico. Through the review of related publications, this work points out studies aimed at the determination of extracts or compounds with pharmacological activity in the treatment of diabetes and hypertension. Below we describe research with Mexican plants with antidiabetic and antihypertensive effect.

Plants with antidiabetic properties

Ethnobotanical records in the Medicinal Herbarium of the Mexican Institute of Social Security (IMSS) of plants used for the treatment of diabetes indicate more than 300 species corresponding to 70 families (39). Within the recommended plants is the nopal (*Opuntia joconostle*) (40), *Cecropia obtusifolia*, commonly known as guarumbo or chancarro (41, 42), *Guazuma ulmifolia*, commonly called guácima, guácimo or caulote (43), *Parmentiera aculeata* whose common name is cuajilote (44) and the thunderstrike (*Tecoma stans*) (45).

Table 1 describes some of the plants used in Mexican folk medicine that have been studied in the past 12 years in order to confirm the antidiabetic effect, through the application of extracts or active compounds. Studies are performed using *in vivo* and *in vitro* tests, mainly in animal normglycemic and hyperglycemic (rats, mice and rabbits). The induction of diabetes in animal experiments (insulin-dependent) is carried out with aloxan, streptozotocin, uric acid, dehydroascorbic acid, some quinolones, some salts of magnesium and hormones such as epinephrine, glucagon, ACTH, somatotropin and pituitary extract (46). They are also used such as Zucker rats genetically obese hyperglycemic animals *fa/fa* (47), yellow mouse KK (48) and spontaneous diabetes in mice of strain C57BLKsj-dbdb (49). Studies are carried out *in vitro* in Caco-2 cells, adipocytes and myocytes L6 (50).

Plants with antihypertensive properties

Different plants with antihypertensive properties are used in Mexican folk medicine, example of them are ternstroemia flowers (*Ternstroemia mutis*), passion flower (*Passiflora suberosa*) and white sapote (*Casimiroa edulis*) (1). Investigations of medicinal plants with properties antihypertensive in Mexico are scarce in comparison to those made with the antidiabetic plants, although from 2010 has increased the interest in studying this type of plants. Table 2 describes the results of research from 2005 to date, shows that between 2000 and 2005 investigations for this purpose is scarce. The results of these studies show that extracts or active principles of some plants used as antihypertensive, present antihypertensive activity or they regulate mechanisms related to arterial blood pressure, such is the case of *Casimiroa edulis* (White sapote, Rutaceae), *Guazuma ulmifolia* (Guásima, Sterculiaceae), *Lepechinia caulescens* (Bretónica, Lamiaceae) and *Agastache mexicana* (Toronji, Lamiaceae). Also shown antihypertensive properties in the orchids *Laelia autumnalis* and *Laelia anceps* and in trees like *Jacaranda mimosaefolia*

(Jacaranda, Bignoniaceae) and *Cochlospermum vitifolium* (Pongolote, Cochlospermaceae).

To carry out the studies of the effect antihypertensive of plant extracts, or their active ingredients, *in vivo* and *in vitro* tests are used. Normotensive, spontaneously hypertensive (SHR) and hypertensive induced L-NAME (Nitro-L-arginine-methyl-Ester) rats are generally used in *in vivo* tests. The *in vitro* tests are performed in cell systems, tissues and isolated organs. Isolated aortic rings are used to determine the effect of extracts or compounds active on á-receptor blockers, blockers of calcium channels, the beta receptor blockers, mechanisms dependent or independent of the vascular endothelium, angiotensin-converting enzyme inhibitors and angiotensin II antagonists (51, 52).

In our working group will carry out research with two plants used in Mexican folk medicine, *Eryngium carlinae* (grass of the toad, Apiaceae) and *Justicia spicigera* (muicle, Acanthaceae) to determine their antidiabetic and antihypertensive properties, respectively. *E. carlinae* inflorescences ethanol extracts in diabetic rats induced by streptozotocin have shown to have an antihyperlipidemic effect, showing the decrease in triglycerides and cholesterol (16). Different types of extracts derived from aerial parts of *Justicia spicigera* have been tested to determine the antihypertensive effect. The results show that chloroform extract has the ability to decrease the values of blood pressure in male hypertensive Wistar rats induced with L-NAME (unpublished data). Both investigations are carried out in order to determine the active principles as well as the mechanism of action.

Conclusion

The severity of diabetes mellitus and hypertension *per se*, as well as its complications and the global increase of the affected people motivate the research and search for new drugs that help control. Mexican ethnobotany offers the scientific study of plants used empirically to validate experimentally the effects.

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Plant species (Part used)	Extracts or Active principles	Ref.
Psacalium decompositum (root)	Aqueous	(53)
Parmentiera edulis (fruit)	Chloroformic	(44)
Cirsium pascuarense (leaf)	Hexanic	(54)
Bidens pilosa (whole plant)	Aqueous-Ethanolic	(28)
Salvia officinalis (whole plant)	Aqueous-Ethanolic	(43)
Cecropia obtusifolia (leaf)	Chlorogenic acid	(41)
Agarista mexicana (stem)	12-ursene-dimethyl-ethyl-stigmastene	(55)
Psacalium radulifolium (root)	Methanolic	(56)
Acosmium panamense (bark)	Buthanolic	(57)
Hintonia standleyana (bark)	3-β-d-glucopyranosyl-23,24-dihydro-cucurbitacin F	(58)
Colubrina elliptica (bark)	Aqueous	(59)
Hintonia standleyana (leaf) *Hintonia latiflora* (leaf)	Phenyl-coumarin 1 Phenyl-coumarin 2	(60)
Agastache mexicana (aerial parts)	Tilianine	(61)
Tecoma stans (leaf) *Teucrium cubense* (leaf and stem)	Aqueous Aqueous	(62)
Prosthechea michuacana (pseudobulb)	Hexanic	(63)
Ibervillea sonorae (root)	Aqueous	(64)
Psittacanthus calyculatus (aerial parts)	Methanolic	(65)
Hylocereus ocamponis (fruit)	Betanidin	(66)

Table 1. Some medicinal plants of Mexico with antidiabetic properties over the period of 2000-2012 researches

Plant species (Part used)	Extracts or Active principles	Assay methods	Ref.
Jacaranda mimosaefolia (leaf)	Aqueous-Ethanolic	Normotensive rats	(67)
Lepechinia caulescens (aerial parts)	Methanolic Ursolic acid	Aortic rings Wistar rats	(68)
Guazuma ulmifolia (bark)	Procianidine fraction	L-NAME rats	(69)
Laelia autumnalis (aerial parts)	Methanolic	Aortic rings SHR rats	(70)
Struthanthus venetus (leaf)	Aqueous-Methanolic	Aortic rings Wistar rats	(71)
Casimiroa edulis (leaf)	Aqueous	Angiotensin II in L-NAME rats	(72)
Agastache mexicana (aerial parts)	Tilianine	SHR rats	(61)
Cochlospermum vitifolium (bark)	Methanolic	SHR rats	(73)
Citrus limetta (leaf)	Aqueous	Angiotensin II in mice	(74)
Salvia elegans (whole plant)	Aqueous-Ethanolic	Angiotensin II in mice	(75)
Laelia anceps (roots)	Methanolic	SHR rats	(70)
Lepechinia caulescens (aerial part)	Methanolic	SHR rats	(76)

Table 2. Mexican medicinal plants with antihypertensive properties over the period 2005-2012 researches