ARTÍCULO ORIGINAL

Plants considered useful for hypoglycemic, antihypertensive or hypolipidemic treatments by patients with peripheral vascular diseases

Plantas consideradas útiles como hipoglicemiantes, antihipertensivas o hipolipemiantes por pacientes con enfermedades vasculares periféricas

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ABSTRACT

Introduction: knowing patients 'believes about the medicinal utility of plants may provide a basis for educating them for a rational use of herb preparations.
Objective: to characterize the plants that are considered useful for antidiabetic, antihypertensive or hypolipidemic treatment among patients with peripheral vascular diseases.
Methods: a survey was performed among patients of the National Institute of Angiology and Vascular Surgery from February through April 2007. The characteristics of the use of plants as medicinal remedies and the names of species considered useful for the treatment of diabetes, arterial hypertension and dyslipidemia were recorded.
Results: two hundred and forty five both sex adult volunteers (142 female/103 male), aged 44 to 72 years) were included in the study. More than 80 % of them used medicinal plants at least occasionally and confided on their efficacy to treat different illnesses Fifteen species, mainly *Allium sativum* L., *Citrus aurantifolia* Ch., *Justicia pectoralis* Jacq.*., Morinda citrifolia* L.*., Ocinum sanctum* L and *Salvia officinalis* L, from 11 botanical families, were mentioned by participants**.** Most patients' claims about plants´ properties have been scientifically supported in some extent, nevertheless, the majority of the pharmacological evidence relays on pre-clinical studies and results of clinical trials are not conclusive. The lack of standardized plant preparations with identified active principles and demonstrated clinical effectiveness are limitations for recommending their therapeutic use.

Conclusion: this study has provided the first characterization of the use of plant products by patients with peripheral vascular diseases for medicinal purposes and confirmed that physicians should be aware about the possibility of herb-drug interactions that should be diagnosed. This information would aid the scientifically supported integration of Phytotherapy to the clinical practice.

Key words: medicinal plant, herb medicine, Diabetes mellitus, arterial hypertension, dyslipidemia, glucose, cholesterol, atherosclerosis, atherothrombosis.

RESUMEN

Introducción: el conocimiento tradicional de los pacientes sobre la utilidad de las plantas medicinales puede servir de base para su educación en el uso racional de las preparaciones herbarias.
Objetivo: caracterizar las plantas que los pacientes con enfermedades vasculares consideran útiles para el tratamiento de la diabetes, la hipertensión y como hipolipemiante.
Métodos: se realizó una encuesta a los pacientes del Instituto Nacional de Angiología y Cirugía Vascular entre febrero y abril de 2007. Las características del empleo de las plantas con fines medicinales y los nombres de las especies consideradas útiles para tratar la diabetes, la hipertensión arterial y la dislipidemia fueron tabulados.
Resultados: doscientos cuarenta y cinco adultos voluntarios de ambos sexos (142 femeninos/103 masculinos, edad 44 a 72 años) fueron incluidos en el estudio. Más del 80 % de ellos utilizaban las plantas medicinales al menos ocasionalmente y confiaban en su eficacia para tratar diferentes enfermedades. Quince especies, fundamentalmente *Allium sativum* L., *Citrus aurantifolia* Ch., *Justicia pectoralis* Jacq., *Morinda citrifolia* L., *Ocinum sanctum* L. y *Salvia officinalis* L., pertenecientes a 11 familias botánicas, fueron mencionadas por los participantes en la encuesta. La mayoría de los planteamientos de los pacientes sobre las propiedades de estas plantas tienen algún fundamento científico, sin embargo, las evidencias farmacológicas disponibles son fundamentalmente de tipo pre-clínico y los resultados de los ensayos clínicos efectuados no son concluyentes. La carencia de preparaciones derivadas de plantas estandarizadas, con principios activos identificados y efectividad clínica demostrada, son limitaciones para recomendar su utilización terapéutica.
Conclusiones: esta es la primera caracterización del uso de productos de plantas con fines medicinales por pacientes con enfermedades vasculares periféricas, y confirma que los facultativos deben conocer sobre la posibilidad de interacciones planta-medicamento que deben ser diagnosticadas. Esta información ayudaría a la integración de la Fitoterapia a la práctica clínica sustentada científicamente.

Palabras clave: planta medicinal, medicina herbaria, Diabetes mellitus, hipertensión arterial, dislipidemia, glucosa, colesterol, aterosclerosis, aterotrombosis.

INTRODUCTION

Atherosclerosis is a silent and chronic inflammatory process at the artery wall that reduces the arterial lumen, the blood flow inside it and the oxygen supply to the affected organs. Secondary to atherosclerotic plaque disruption a procoagulant state may arise leading to the occurrence of acute arterial thrombosis (atherothrombosis). The clinical consequences of these events (myocardial infarction, stroke or lower limb occlusive disease) are responsible for high number of deaths and disabilities worldwide. The progression of the atherosclerotic plaque and occurrence of its clinical manifestations are directly related to the oxidation of lipids in low dense lipoproteins (LDLs) that become trapped in the extracellular matrix of the subendotelial space.[1]

Diabetes mellitus, arterial hypertension and dyslipidemia are risk factors for atherothrombosis and different drugs are used for their pharmacological control,[2-4] However, the need for effective, safe and low-cost therapeutic options that contribute to the quality of life of the growing number of subjects who suffer from these diseases is still a problem and people has empirically looked for herb remedies to relieve their clinical symptoms.[4-7] However, it has been suggested that physicians should be alert about the possibility of adverse effects due to concomitant intake of conventional drugs and herb remedies and ask their patients about the use of these products.[8]

Since patients with peripheral vascular diseases, mainly those with arterial diseases[9] are likely to suffer from Diabetes mellitus, arterial hypertension and dyslipidemia, knowing their believes about the medicinal utility of plants may provide a basis for educating them for a rational use of herb preparations. In consequence, this work was aimed to characterize the plants that are considered useful for antidiabetic, antihypertensive or hypolipidemic treatment among this group of patients.

METHODS

Adult patients with peripheral vascular diseases admitted to the medical care units of the National Institute of Angiology and Vascular Surgery were included in a survey aimed to determine the medicinal plants that they considered useful for the treatment of diabetes, arterial hypertension and hypercholesterolemia.

Sample size calculation

Ten percent of the average number of patients who attended each single unit in a three-month period was considered an appropriate sample of institutional attendees for the stated purpose. These figures were: 100; 65 and 80 for Diabetic Angiopathy, Arteriology and Phlebo-Lymphology units, respectively. Thus, 245 was the whole number of patients to be included in the study.

Patient inclusion strategy

Ambulatory and hospitalized patients from each medical unit were included in the study from February through April, 2007, according to a randomized blocks method. They were interviewed about the following issues:

- Frequency of the use of medicinal plants (seldom, occasionally or often).
- Level of confidence on the effects of medicinal plants (low, moderate or high).
- Known medicinal plants (common name) useful for the treatment of Diabetes mellitus, arterial hypertension or high blood lipids.
- Type of herb preparation more frequently used (domestic or pharmaceutical).

Ethics

This study was done according to a research protocol previously approved by the Ethics Committee and the Scientific Council of the National Institute of Angiology and Vascular Surgery.

The objective and the characteristics of the investigation were explained to the patients and their informed consent obtained before their inclusion in the study.

Quality assurance of the study

A group of nurses of the three medical care units were trained to perform the survey and informed on topics regarding medicinal plants nomination. Protocol adherence and the quality of the information recorded in a data base were systematically double-checked by two researchers.

Statistical analysis

The data are expressed as absolutes values and percentages.

RESULTS

Included patients demographic characteristics

The research protocol was accomplished according to the plan. Two hundred and forty five both sex adult volunteers, were included in the study. The majority of them had a secondary or higher level of education and was socially active persons that lived in Havana or in the two nearest provinces to it (table 1).

Table 1. Included patients 'demographic characteristics

N	245 (142 F / 103 M)
Age Mean (range)	61 (44 to 72)
Province of residence	N (%)
Havana	155 (63,3)
Artemisa/Mayabeque	46 (18,8)
Other	44 (17,9)
Education	N (%)
Primary	47 (19,2)
Secondary school	72 (29,4)
High School	73 (29,8)
University	53(21,6)
Occupation	N (%)
Worker	98 (40,0)
Retired	59 (24,1)
Housewife	88 (35,9)

Use of medicinal plants by patients with peripheral vascular diseases

More than 80 % of participants used medicinal plants at least occasionally and confide on their efficacy to treat different illnesses either as domestic remedies or pharmaceutical herb preparations (table 2).

Table 2. Use of medicinal plants by patients with peripheral vascular diseases

Frequency of use of medicinal plants	N (%)
Seldom	52 (21,2)
Occasionally	120 (48,9)
Often	73 (29,8)
Level of confidence on the effects of medicinal plants	N (%)
Low	41 (16,7)
Moderate	105 (42,8)
High	99 (40,4)
Type of herb preparation more frequently used	N (%)
Domestic	117 (47,8)
Pharmaceutical	128 (52,2)

Plants considered useful for the treatment of Diabetes mellitus (DM), arterial hypertension (HT) or high blood lipids (DL) by patients with peripheral vascular diseases

The number of reports recorded regarding plants considered useful to treat diabetes, hypertension and hypercholesterolemia were 120; 155 and 215 respectively. Fifteen plant species from 11 botanical families were mentioned by the participants in the study. *Ocimum tenuiflorum L.*, *Morinda citrifolia* L. and *Allium sativum* L. were the most reported plants among those with attributed

hypoglycemic effect. *Allium sativum* L., *Justicia pectoralis* Jacq. and *Citrus aurantifolia* Ch., were the most mentioned within the group of plants considered good for blood pressure lowering, while *Morinda citrifolia* L., *Salvia officinalis* L. *and Allium sativum* L . had the highest number of reports among plants appreciated as blood cholesterol reducers (table 3).

Table 3. Plants considered useful for the treatment of Diabetes mellitus (DM), arterial hypertension (HT) or high blood lipids (DL) by patients with peripheral vascular diseases

Scientific name (Family)	Popular name in Cuba	DM N (%)	HT N (%)	DL N (%)
Allium sativum L. (Liliaceae)	Ajo	21 (18)	36 (23,2)	51 (23,7)
Allophylus comini (L,) Sw (Sapindaceae)	Palo de caja	1 (0,8)	-	-
Artocarpus altilis (Parkinson) Forberg (Moraceae)	Árbol del Pan	1 (0,8)	-	-
Citrus aurantifolia Ch, (Rutaceae)	Limón	-	29 (18,7)	-
Citrus aurantium L, (*Rutaceae*)	Naranja agria	-	6 (3,8)	-
Citrus paradisi L, (Rutaceae)	Toronja	-	4 (2,6)	-
Cymbopogon citratus (DC,) Stapf (Poaceae)	Caña santa	-	8 (5,3)	-
Justicia pectoralis Jacq, (*Acanthaceae*)	Tilo	-	33 (21,3)	-
Morinda citrifolia L, (Rubiaceae)	Noni	40 (33,3)	17 (11,0)	59 (27,4)
Ocimum tenuiflorum L, (*Lamiaceae*)	Albahaca Morada	52 (43,3)	21 (13,5)	-
Orthosiphon aristatus Blume, (Lamiaceae)	Té de riñón	-	1 (0,6)	-
Persea americana Mill, (Lauraceae)	Aguacate	-	-	15 (7,0)
Plantago major L, (Plantaginacea)	Llantén	5 (4,2)	-	5 (2,3)
Salvia officinalis L, (Lamiaceae)	Salvia de Castilla	-	-	55 (25,6)
Solanum melongena L, (Solanaceae)	Berenjena	-	-	30 (14,0)
Total number of reports/use	-	120	155	215

DISCUSSION

This work has provided the first characterization of the use of plant products by patients with peripheral vascular diseases for medicinal purposes and has demonstrated the usefulness of this kind of studies.

Most patients claims about the beneficial properties of plants have been scientifically supported. Nevertheless, the majority of the pharmacological evidence available relays on pre-clinical studies and the results of the clinical trials performed are not conclusive.[10-12] In addition, some information gaps and contradictory facts, like those described below, are limitations to assure that some of them would be clinically effective in humans.

For instance, it has been reported the use of *Solanum melongena* L. fruit aqueous macerates as natural remedies for hypercholesterolemia in Cuba,[13] however, as far as we know, there is no scientific evidence that support this practice. Besides, the results of the evaluation of other types of preparations from this species are variable. Thus, oral administration of fresh, ripe fruits to rabbits under atherogenic diet significantly reduced serum concentrations of total cholesterol, triglyceride, LDL-cholesterol, increased HDL-C and HDL/LDL- C ratio and decreased hepatic lesions.[14] However, ad libitum intake of *S. melongena* fruit aqueous extract provoked serum cholesterol increase and hepatic cholesterol decrease in rats under hypercholesterolemic diet without influence on circulating and tissue triglyceride levels.[15] Furthermore, serum total cholesterol and atherogenic lipoproteins, as well as aortic lesion area were unaffected, while oxidative stress markers were elevated in LDLR (-/-) mice fed atherogenic diet treated with a fruit extract.[16] Moreover, a double-blind placebo-controlled study with hypercholesterolemic human volunteers demonstrated significant reduction of blood levels of total and LDL-cholesterol and of apolipoprotein B after daily intake of a dried powder fruit infusion, however these changes were similar to those achieved when patients accomplished dietary changes and exercise activities.[17] Besides, oral intake of dried powdered fruits failed to decrease serum total cholesterol, LDL- cholesterol and LDL/HDL during another double-blind placebo-controlled study with hyperlipidemic volunteers.[18] Therefore, the possible hypolipidemic effects of *S. melongena* fruit aqueous macerates should be assessed.

Plantago major L. is another example, since a single oral dose of *P. major* leaf crude aqueous extract was unable to prevent hyperglycemia in rats during the glucose tolerance test [19]. However, lower blood cholesterol levels and atherosclerotic lesions in aorta were demonstrated in rabbits treated with a leaf extract given concomitantly with a hypercholesterolemic diet.[20] Thus, suggesting a hypolipidemic but not a hypoglycemic potential of products derived from this species.

Finally, patients´ believes with respect to the utility of *Citrus aurantifolia* Ch. and *Justicia pectoralis* Jacq. for hypertension control agrees with Ethnomedical reports[21,22] but scientific evidence is missing.

This study has led to the identification of botanical species that could be candidates for the development of plant preparations useful as complementary therapies for Diabetes mellitus, arterial hypertension and dyslipidemia. Pharmaceutical products from three of these species (*Allium sativum* L., *Justicia pectoralis* Jacq. and *Orthosiphon aristatus* Blume) are included in Cuban Ministry of Health's Formulary of Phyto pharmaceutical products from[23-25] and their hypoglycemic, anti-hypertensive and/or hypolipidemic efficacy should be demonstrated during clinical studies with patients who would benefit from these treatments.

Similar preparations should be developed from the other species mentioned by the interviewees that have been accepted for their medicinal use in Cuba[26] (*Citrus aurantifolia* Ch., *Cymbopogon citratus* (DC.) Stapf, *Morinda citrifolia* L., *Ocimum enuiflorum* L., *Plantago major* L. and *Salvia officinalis* L.) and pharmacologically assessed in pre/clinical and clinical conditions. Nevertheless,*Allophylus comini* (L.) Sw., *Artocarpus altilis* (Parkinson) Forberg, *Citrus paradisi* L. *Persea americana* Mill. and*Solanum melongena* L., should not be excluded from a research plan, since, they are used in Cuba as medicinal and /or edible plants.[13,22,27,26,29]

The scientific evidence available suggests that some herb remedies that patients with peripheral vascular diseases consider therapeutically useful could, in fact, be pharmacologically active. Thus, pharmacological interactions between these products and conventional drugs may be expected. Therefore, physicians should be aware about this possibility that should be diagnosed. This information would aid the scientifically supported integration of Phytotherapy to the clinical practice.

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