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Ethnomedical and Ethnopharmacological Study of Plants Used by Indigenous People of Cameroon for The Treatments of Diabetes and its Signs, Symptoms and Complications

Tsabang N[1,3,4]*, Fongnzossié E[2], Keumeze V[3], Jiofack R[4], Njamen D[5], Sonwa DJ[6] and Nguelefack Benois Telesphore[7]

[1]*Institute of Medical Researches and Medicinal Plants Studies (IMPM), PO Box 6163Yaoundé, Cameroon*
[2]*University of Douala, Cameroon*
[3]*Ecologic Museum of millennium, Yaounde Cameroon*
[4]*Institute of environment Sciences, Yaounde, Cameroon*
[5]*University of Yaoundé I, Faculty of Sciences, Yaounde, Cameroon*
[6]*Center for International Forestry Research (CIFOR), Yaounde, Cameroon*
[7]*University of Dschang, Dschang, Cameroon*

Abstract

Diabetes is one of the most important multifactorial, metabolic and chronic diseases, with fatal complications that remain a public health problem worldwide. The estimations by the international diabetes federation (IDF) showed in 2015 that, 415 million people had diabetes and with an expected rise to 646 million in 2040. Many ethnobotanical surveys were carried out in several parts of the world, but none has investigated the ethnomedical surveys to record plants used for both treatments of diabetes and its derived manifestations. Therefore, the objective of the present study was to collect and document information on herbal remedies traditionally used for the treatment of diabetes and its signs, symptoms and complications in Cameroon. Detailed botanical prospection and ethnopharmacological thorough preparation was conducted nearby 1131 interviewers from 58 tribes of Cameroon, in a random distribution. In total, 103 plant species belonging to 72 genera in 34 families were reported to be used in the preparation of the herbal remedies. The following species that include *Antrocaryon klaineanum, Entandrophragma cylindricum, Cylicodiscus gabunensis, Allanblacka floribunda* and *Glossocalyx brevipes* are amongst many recorded plants documented for the first time in the treatment of diabetes and its interconnected diseases. Nineteen plants species including *Allium cepa, A. sativum*, *Momordica charantia, M. foetida, Morinda lucida* are recognized by some interviewers in both usual and suspected treatment of diabetes. *Abrus precatorius, Dioscoreophyllum volkensis, Synsepalum dulcificum* and *Thaumatoccus daniellii* are known as edulcorants endowed of antidiabetic properties. The results provide the base for herbal medicines used in diabetes management and for further preparation of phytodrugs for diabetes and its complications.

Keywords: Indigenous people of Cameroon; Ethnomedical and ethnopharmacological study; Treatment of diabetes and its signs; Symptoms and complications

Introduction

Diabetes mellitus, one of the leading causes of death affecting over 100 million people worldwide, is the multifactorial, commonest non-communicable endocrine disease characterized by hyperglycemia and disturbances in carbohydrate, protein, and lipid metabolism, due to absolute or relative deficiency in insulin secretion or insulin action. The estimations by the international diabetes federation (IDF) showed that in 1985, 30 million people had diabetes with the number that rose to 150 million in 2000 and 246 million in 2007, with projection made by IDF that towards 2025, the number would have risen to 380 million [1]. IDF had discovered that this number was already exceeded in 2015; therefore, the global prevalence was 415 million people with diabetes and by 2040 from that will rise to 642 million [2]. The African continent has the highest proportion of undiagnosed diabetes; over two thirds (66.7%) of people with diabetes are unaware they have disease [2]. Many health tradipratitioners in Africa don't know this metabolic disorder. Meanwhile, they treat some of its signs which include severe and sustained physical and psychic asthenia; its symptoms which include visual disturbances and its complications that include retinopathy, nephropathy, neuropathy, ulcer gangrene and arteriosclerosis. Today diabetes is a pandemic with destructive effects in poor and intermediary income countries. Type 2 diabetes affects actually 300 million people in the world, which represents 6.6% of adult population. Seven million other people add each year with children not exempted. A half-million of less than 15 years old children are attacked by type 1 diabetes, more of the half of them living in poor countries [3].

In Cameroon, this chronic metabolic pathology affects more than 10% of the urban population. Ninety percent (90%) of patients are types 2 diabetic (non-insulin-dependent) [4]. IDF has estimated that Africa Region spent about USD 3.4 billion to USD 5.9 billion only on diabetes healthcare in 2015, the lowest expenditure of any region [2]. Fortunately, hinterland population, living far of urban centers rich in manufactory hypoglycemic drugs and hospitals, have developed a great experience on the uses of medicinal and food plants. In response to the global health challenge, the WHO expert Committee on diabetes recommended further evaluation of the folkloric methods of managing this disease and its signs, symptoms and complications; because of the

***Corresponding author:** Tsabang Nole, Center for Research on Medicinal Plants and Traditional Medicine, Institute of Medical Research, and Studies of Medicinal plants (IMPM), Ministry of Scientific Research and Innovation Yaounde, Cameroon, Tel: +237678017339; E-mail: tsabang2001@yahoo.fr

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high mortality and the morbidity arising from its complications and the draw-backs associated with the use of conventional hypoglycemic drugs [5]. Therefore, the present work has investigated the plants used in traditional medicine for the treatment of diabetes in Cameroon and for their scientific valorization.

Methodology

Ethnomedical diabetes description

The ethnomedical and ethnopharmacological survey was carried out nearby health tradipractioners, householders and diabetic patients. These interviewers were divided into groups. The first group constituted of interviewers who don't know diabetes, but treat it through its signs, symptoms and complications which were identified with the assistance of a physician. The second group concerns the interviewers who know diabetes. Early signs or symptoms as sexual weakness, headache**,** dizzy, excessive perspiration, etc. were recorded. Some of diabetic complications recorded are: cardiac problems (arteriosclerosis), chronic *renal insufficiency*, obesity, fungi skin infections, blindness, etc.

Identification of recorded plants

Samples of plants used to treat diabetes and its interconnected diseases were harvested, identified and confirmed in national herbarium of Cameroon**.**

Ethnopharmacological preparation

The ethnopharmacological preparation of recipes derived from recorded plants were described in detail with the precision of the specific part (s) of plant (s) used either fresh or dry and the quantity of material for an ethno pharmacological preparation, the precision of the composition of the recipes that may be only a mixture of plants and/or a mixture of plants and non-plant resources like minerals or animal. The precision was also done on the ethno medical routes of administration (oral, topical, scarification, rectal). The mixture was either simultaneously or sequentially taken. The quantity of water or other solvent used, the temperature of ebullition and the time of preparation were taken in consideration. The administration of the preparations were also described with the precision of the amount of medicine used per dose, per day, the duration of treatment, the undesirable effect (s), the secondary effect (s) and the associated or forbidden food (s). The ethnopharmacological and the ethnomedical data collection field form was used to collect data. The verification of antidiabetic activities and plant mechanisms of action were assessed through bibliography research. The hyperglycemic regulation is ensured by a great number of plants with different mechanisms which differed according to the types of diabetes and their causes.

Statistical analysis

The interviewers which include group 1 constituted of informants who don't know diabetes and arterial hypertension, but treat them through its signs, symptoms and complications and group 2 constituted of informants who know diabetes and arterial hypertension; were compared using the comparison of a percentage based on a large sample of size n>30 with a known standard. The ethnopharmacological preparation modes of recipes which include decoction, maceration, infusion and consumption were classified in two groups that were compared. The first group was constituted by the number of times the decoction was used and the second group was constituted by the sum of the rest of the ethnopharmacological modes of preparation of recipes [6].

Results

Distribution of the recorded results

In total, 103 species of plants belonging to 72 genera in 34 families were reported to be used in the preparation of the herbal remedies. Many signs, symptoms and complications of diabetes and correspondent plant species for their treatment were recorded. About 10 different mechanisms of action of medicinal recorded plants, toxicity of some medicinal plants and precautions necessary during the use of antidiabetic plants are presented in this work. *Abrus precatorius, Dioscoreophyllum volkensis, Synsepalum dulcificum* and *Thaumatoccus daniellii* are both antidiabetic and edulcorants or sweatening agents.

Ethnomedical study and medicinal important properties of recorded plants

Protective role of medicinal plants on the onset of diabetes: Type 2 diabetes, detected early can be retarded by anti-obesity plants. These plants can regulate the overweight sometime responsible of the disease.

Some cases of confusions to avoid

Sometime, vernacular names of plants design more than one plant species that belong to different genera or different families. These are some cases of possible confusions to be avoided. Tanga is the vernacular name of *Rhizophora racemosa* in Douala and *Vepris louisii* in Baka. *Entandrophragma candollei* and *Amphimax pterocarpoides* are called Kanga in Baka. Etoup is vernacular name of *Treculia africana* and *Sterculia tragantha* in Ewondo. Tim in Badjoue is the name of *Strombosia pustulata* and *Strombosiopis tetrandra*. Nkam in Badjoue is the name of genus Celtis and *Fernandoa adolfi-friderici.* Ossie is the genus' name of Entandrophragma in Badjoue. Assam the genus' name of Uapaca in Ewondo, Bulu and Fang. Essok and Gambe are vernacular names of species of *Garcinia* respectively in Ewondo and in Baka. Oyale-zom is a vernacular name, common to genus Momordica in Ewondo. Ossa'a and Ossom are Badjoue's name of respectively genus Albizi*a* and Uapaca [7].

Hypoglycemia alarm signs of diabetes

Hypoglycemia appears when the glycemia in fasting is inferior to 0.66 g/l. Diabetic patients must imperatively stop the treatment since the appearance of the following signs: perspiration, mental trouble, shivering, dizzy, nervosity, irritability, increasing heart beat and feeling drunk. Since the appearance of those signs, it recommends to stop the treatment and to take a sweet food and sweet drink.

Ethnopharmacological study of recorded plants used by indigenous people

In Supplementary Table all the interconnected signs, symptoms and complications of diabetes are indicated and all the recorded recipes are described. All the recorded plants are classified alphabetically after the plant names according to the four different ethnopharmacological modes of preparation that include decoction; maceration; infusion and consumption.

The Supplementary Table shows that there are 4 main categories of recipes, corresponding to 103 plant species. Ten of these plant species including *Andira inermis*, *Staudtia kameroonensis, Treculia africana*, *Angylocalyx talbotii, Margaritaria discoidea, Corchorus olitorius*, *Chamaecrista mimosoides*, *-Ipomoea mauritiana, Eclipta prostate* and *Glossocalyx brevipes,* provide 11 supplementary recipes that include 10 applications of powder or pasta on the skin and consumption.

Therefore, a total of 114 recipes that correspond to five main ethnopharmacological modes of preparation were recorded. Seventy-four (74) of them were decoction, 15 macerations, 11 infusions, 11 simple applications of pasta, liquid, leaves or powder on the skin and 3 are consumption or eating.

Comparison between the two groups of interviewers

The survey reveals two groups of informants. The group of 340 interviewers, who don't know diabetes, but treat them through its common signs, symptoms and complications and the group of 791 interviewers who know diabetes. We have used the comparison of a percentage based on a large sample of size n>30 with a known standard that involves a binomial distribution. We find 340 of people who don't know diabetes out of a total of 1131 informants. The variance of this test is v=pq/1131= ½ × ½ /1131=0.0002 and the standard error is $\sqrt{pq/n}$=0.0148. The departure of the observed value 340/1131=0.3006 or 791/1131=0.6993 from the hypothetical value 0.5000 is 0.5000-0.3006=0.1994 or 0.6993-0.5000=0.1993, which is in the two cases appreciably greater than 2, 6 times the corresponding standard error. According to the definition we conclude that there is significant evidence between the two groups at the 5 per cent level. The people who know diabetes are more important than those who do not know it. The survey was conducted more in towns, where many people know diabetes through the contact with many diabetic patients, the frequentation of hospitals and the influence of medical doctors.

Comparison between different types of ethnopharmacological modes of recipes' preparation

The survey revealed seventy-four (74) cases of decoction; 15 cases of macerations; 11 cases of infusions, 11 cases of simple applications of pasta, liquid, leaves or powder on the skin and 3 cases of consumption or eating. We want to demonstrate that the decoction is dominant than the four other ethnopharmacological modes of preparation of recipes (15+11+11+3=40).

We have now two groups, the group of 74 cases of decoction and the group of the other ethnopharmacological modes of preparation of recipes. We have used the comparison of a percentage based on a large sample of size n>30 with a known standard that involves a binomial distribution. We find 40 of ethnopharmacological modes of preparation of recipes constituted the first group out of a total of 114 recipes. The variance of this test is v=pq/114=½ × ½ /114=0.0022 and the standard error is $\sqrt{pq/n}$=0.0468. The departure of the observed value 40/74=0.3508 or 74/114=0.6491 from the hypothetical value 0.5000 is 0.5000-0.0022=0.1492 or 0.6491-0.5000=0.1491, which is in the two cases appreciably greater than 2, 6 times the corresponding standard error. According to the definition of the test we conclude that there is significant evidence between the two groups at the 5% level. In the ethno pharmacological preparation of diabetes herbal medicine, the decoction is widely dominant in Cameroon. People use more stem bark than other parts of plants and their rapid extractions need much heat.

Discussion

Antidiabetic effect of medicinal recorded plants and their mechanism of action

Chemical compounds and their pharmacological activities: The previous pharmacological tests proved that some recorded plants possessed antihyperglycemic activities. They are presented in Table 1.

The Table 1 shows that plants possess active substances responsible of several hypoglycemic properties.

Scientific names	Active constituents	Activities
Allium cepa	Allyl propyl, allicine, Glycosides, kampferol, Acethylpropyldisulphil, Quercetin	Hypocholesterolemic Peripheric vasodilatator, Diuretic,
		β cells stimulation [8,9]
Allium sativum	sulfuric organic Compounds	Hypocholesterolemic, Peripheric vasodilatator Diuretic, calcium inhibitor
		β cells stimulation [9]
Anacardium occidentale	Aqueous extract of bark and leaves, kampforol, quercetol	Peripheric vasodilatator [10]
		β cells stimulation [11]
Catharanthus roseus	Catharantin; lochnerin, tetrahydroalstorin, leurosin sulphate, vindolin	β cells stimulation
Phyllanthus niruri	Phyllanthin, hydrophyllanthin, 4 alchaloïds, quercetoside, norsecurins isomers and lupeol [10]	β cells stimulation
Solanum melongena	Trigonellin, cafeic acide, cholin [12]	β cells stimulation
Momordica charantia, *M. foetida*	Phytosterin glycosides: charantin, momordicin, foetidin	β cells stimulation, Facilitated penetration of glucose in cells, Oral glucose tolerance Increase glycogen synthesis [8]
Spathodea campanulata	Aqueous extract	Facilitated penetration of glucose in cells [13]

Table 1: Recorded plants and their hypoglycemic effects.

The good knowledge of recorded plants' mechanisms of action described below can help in the management of diabetes and its interconnected diseases.

From a practical standpoint recorded plants are used for the control of three main types of diabetes: type 1 diabetes in which the pancreas contains little or none beta cells, type 2 diabetes in which beta cells are available and gestational diabetes in pregnancy. These different diseases correspond respectively to juvenile diabetes, adult diabetes and hyperglycemia in pregnancy. The islet tissue in adult diabetics contains more available beta cells and by consequent they produce insulin with the averages up to 30% of normal. Then among recorded plants some can either be insulinotropic (increased insulin release from pancreatic beta cells), or present insulin mimetic activity (peripheral hypoglycemic effect) and may have both properties. Allyl propyl disulphide (APDS) extracted from *Allium cepa* (onion) removes insulin inactivation [8-14]. Also, S-methylcysteine and quercetin have induced their antidiabetic effects by decreasing the onset of hyperglycemia and lipid profiles, increased antioxidant activity by reducing lipid peroxidation and oxidative stress. Extract of onion has also induced its antidiabetic effects by decreasing liver enzymes and increasing antioxidative activity [15]. *Momordica foetida* and *Spathodea campanulata* produce anthocyanosides that might facilitate the penetration of glucose in cells for combustion [16-18]. Leaves aqueous extract of *Mangifera indica* shows the hypoglycemic effect due to a reduction in glucose intestinal absorption [19]. The administration of 4oo mg/day of *Gymnema sylvestre* to 27 patients with insulin-dependent diabetes (type 2) enhances endogenous insulin release possibly by regeneration/revitalization of the residual ß-cells [8]. Another recorded species *Allium sativum* protects pancreatic ß-cells by antioxidant activity of its extract [20]. The fruit juice of *Momordica charantia* have significantly reduced the blood glucose level and increased concentration of plasma insulin in diabetic rats. The observed effect was due to an increase in the number of beta cells in treated animals compared to non-treated one

[21]. Therefore, *Momordica charantia* increases the renewal of partial cells in the pancreas. It may permit the recovery of partially destroyed cells and stimulates pancreatic insulin secretion [22]. Allicin, sulfur-containing compound of *Allium sativum* showed to have significant hypoglycemic activity due to increased insulin release from pancreatic beta cells and S-allyl cysteine sulfoxide has shown antioxidant and secretagogues activity [23,24]. Daily oral feeding of garlic extracts at 100 mg/kg increased plasma insulin level with concomitant decrease in plasma glucose levels [25]. Effect of garlic on high-fat diet feed rats for 2 weeks suggests that garlic is insulinotropic rather than hypoglycemic [26]. *Capsicum frutescens* increased serum insulin concentration in a high-fat diet-fed streptozotocin induced type 2 diabetes rats after 4 weeks treatment. The data of this study suggest that 2% dietary *Capsicum frutescens* is insulinotropic rather than hypoglycemic in the experimental methods [26]. The phytochemical momordicin, charantin, and a few compounds such as galactose-binding lectin and insulin-like protein isolated from various parts of this plant have been shown to have insulin mimetic activity [21,27]. Allicin, a sulfur-containing compound showed also to have significant hypoglycemic activity due to increased hepatic metabolism [26]. *Brassica oleracea* has shown a significant hypoglycemic action through the increased activity of glycogen synthetase and decrease in glycogenolysis and gluconeogenesis demonstrated by a decreased activity of glycogen phosphorylase and gluconeogenic enzymes [8]. *Momordica charantia* extract causes a 4-5 fold increase in rate of glycogen synthesis from U-14C in the livers of normal fed rat [26]. Some plants are interesting for diabetic nutrition. Each one of these plants has an edulcorant which is a sugar for diabetics. *Abrus precatorius* has glycyrrizin (a protein 60 times sweeter than saccharose) [8]. *Dioscoreophyllum volkensis* leaves have monolline (a protein 180 times sweeter than saccharose) [8]. *Synsepalum dulcificum* possesses a sweetening agent which is a glycoprotein named miraculin from fruits called miraculin barriers and *Thaumatoccus daniellii* has in the aril around the seeds thaumatin, a sweetening agent 1600 times sweeter than saccharose for some or 4000 times sweeter than saccharose for others [8]. Many studies have validated the traditional use of *Abrus precatorius*, *Synsepalum dulcificum* and *Thuamatococus daneillii* in the management of diabetes mellitus [28,29].

Due to the adverse effects found to some recorded species in the treatment of diabetes the use (in strong doses) of some plants is forbidden to avoid intoxication risks. There are: *Momordica charantia*, *Andira inermis*, *Abrus precatorius* (seeds) and *Senna occidentalis* (seeds unroasted). The strong doses of *Andira inermis* provoke the vomiting, violent purge, delirium, narcosis and mag crisis. The strong doses and the prolonged use are toxic. Pregnant women must avoid taking the treatment with *Momordica charantia* because of its ocitoxic property [30]. The seeds of *Abrus precatorium* are toxic (3 to 4 seeds can kill a horse) [8]. The maceration of *Phyllanthus nurirus* is toxic in strong doses [8]. The use of *Laportea ovalifolia* and *Morinda lucida* is strongly recommended, because of their non-toxicity [31,32,34-37].

Conclusion

This work has presented a list of one hundred and three (103) medicinal plants used for traditional treatment of several signs, symptoms and complications of diabetes. Sixteen amongst them are also recognized by some interviewers as usual antidiabetic plants. Many of them have been documented for the treatment of diabetes and their phytochemical studies revealed the presence of many antidiabetic compounds. The previous pharmacological studies have confirmed the activity of those recorded plants and the rationalization of the traditional Knowledge about the herbal medicine treatment of diabetes. These practices exist mostly in Cameroon's towns where many health tradipractioners recognize this pathology. But hinterland population, living far of urban centers rich in manufactory hypoglycemic drugs and hospitals, have developed a great experience on herbal remedies more accessible, cost effective for indirect treatments of diabetes through its signs, symptoms and complications. Some medicinal plants that include *Allium cepa, Morinda lucida* and *Corchorus olitorius* are used in the treatment of some diabetic interconnected diseases as nervosity, heart palpitations, arteriosclerosis, stroke and renal insufficiency. However, manifold plants used for the treatment of signs, symptoms and complications have not been characterized. More investigations must be carried out to evaluate their effectiveness, mechanisms of action and toxicity before producing phytodrugs cheaper and more effective. The treatment of some complications by natural products will be an advantageous solution in economic standpoint for diabetic patients.

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