Efficacy of Surinamese plants in the therapy of diabetes mellitus - analysis of the literature

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Abstract

Diabetes mellitus is highly prevalent in Suriname, where it claims more than 170 deaths per year. Plant-derived preparations are extensively used in the treatment of this disorder, but often without scientific proof of therapeutic efficacy. In this study, we searched in on-line libraries such as PubMed and Hinari for evidence of potential therapeutic efficacy of Surinamese plants that are commonly used for treating diabetes. The fifteen most frequently mentioned plants were Azadirachta indica (neem), Catharanthus roseus (kotomisi), Desmodium canum (toriman), Mangifera indica (manya), Momordica charantia (busi sopropo), Morinda citrifolia (didibri apra), Orthosiphon stamineus (kattesnor), Phyllanthus niruri (finibita), Physalis angulata (batobobita), Quassia amara (kwasihibita), Ruellia tuberosa (watrakanu), Spondias dulcis (pomme citere), Stachytarpheta jamaicensis (isriwiwiri), Syzygium cumini (dyamun), and Wulffia baccata (sukrutanta). Preparations from A. indica and P. niruri may lower elevated blood sugar levels, but this assumption is only based on a few clinical studies. Those from M. charantia were positive in some clinical studies but negative in others, while those from S. cumini turned out negative in all clinical tests. Preparations from C. roseus, M. indica, M. citrifolia, and O. stamineus have only undergone preclinical evaluation. And those from D. canum, P. angulata, Q. amara, R. tuberosa, S. dulcis, S. jamaicensis, and W. baccata have never been tested. Thus, the scientific evidence to support the clinical use of the above-mentioned plants in the treatment of diabetes is scant. Patients treat their disease with substances that may be ineffective and/or may cause unforeseen adverse effects. The plants should be evaluated in well-designed preclinical and clinical studies to define their roles in the treatment of diabetes.

Key words: diabetes mellitus; Suriname; ethnopharmacological medicines; meta-analysis

Introduction

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia (constitutively elevated plasma glucose concentrations, i.e., fasting plasma glucose > 7.0 mmol/L, or plasma glucose > 11.1 mmol/L 2 h after a meal) as a result of insufficient insulin secretion, insufficient insulin action, or both (World Health Organization, 2006). The defective insulin secretion is the result of inappropriate functioning of the β cells of the pancreas, while the inadequate insulin action is generally associated with resistance of the target tissues to insulin. The hyperglycemia occurs because of uncontrolled glucose release by the liver, reduced uptake of glucose by skeletal muscles, and decreased storage of glucose in the form of glycogen. When the renal threshold for glucose reabsorption is exceeded, glucose spills over into the urine – glycosuria - and causes an osmotic diuresis (polyuria), which results in dehydration, thirst, and increased drinking (polydipsia).

These abnormalities can lead to distinctive acute and chronic complications (Tripathi and Srivastava, 2006) including ketoadidosis (poisoning of the body by ketones produced during the breakdown of fat to generate energy in the absence of glucose), hyperosmolar coma (characterized by disordered mental functioning and sensory or motor impairments caused by hyperviscosity of the blood), macro- and microangiopathy (blockage of the blood flow in the large vessels and leakage of the capillaries, leading to impaired oxygen flow to the tissues, necrosis and gangrene, and amputation and blindness), nephropathy (malfuioning of the kidneys caused by damage to the capillaries in the glomeruli), neuropathy (disturbances in the peripheral nervous system affecting first the nerves of the lower limbs and often affecting autonomic nerves), and recurrent infections (due to weakening of the immune system defenses, nerve damage, and reduced blood flow to the extremities). These complications are the principal causes of illness and death in patients suffering from diabetes mellitus (Tripathi and Srivastava, 2006).

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Diabetes mellitus is among the most widespread non-communicable diseases in many parts of the world, with a global morbidity and mortality in 2011 of 366 million and 4.6 million, respectively (International Diabetes Federation, 2011). These numbers are rising rapidly: in 2010, the global prevalence in adults was 6.4% or 285 million, but it is anticipated to reach 9.9% or 552 million by 2030 (International Diabetes Federation, 2011). During this twenty-year period, the number of adults with diabetes mellitus will increase with 20% in industrialized countries but with 69% in developing countries (Wild et al., 2004; Shaw et al., 2010; International Diabetes Federation, 2011). The latter development is for an important part attributable to continuous growth and aging, rapid urbanization, and an increasing frequency of obesity and physical inactivity in large parts of the Third World (Wild et al., 2004; Shaw et al., 2010; International Diabetes Federation, 2011). Indeed, it is now recognized that it is the low- and middle-income countries that presently face the greatest burden of diabetes mellitus.

This holds probably also true for The Republic of Suriname. According to recent estimates, the prevalence of diabetes mellitus in individuals aged 20 to 79 years was 9.7% in 2007, between 10 and 11% in 2011, and will reach 12.3% in 2030 (International Diabetes Federation, 2008; 2011). This implies that roughly one Surinamese adult in ten suffers from diabetes mellitus, a scenario that is not likely to alter in the near future. Moreover, at least 170 Surinamese diabetics die each year from their disease (Punwasi, 2011), which corresponds on average with three diabetes fatalities per week. This makes this condition the fifth leading cause of death in Suriname, after cardiovascular diseases, external causes, malignant neoplasms, and perinatal calamities (Punwasi, 2011).

The population of Suriname of approximately 530,000 is, among the most varied in the world, comprising inhabitants from virtually each continent (Helman, 1977; General Bureau of Statistics, 2005), all of whom have largely preserved their ethnopharmacological traditions (Helman, 1977). Located on the Guiana Shield, Suriname is generally believed to contain one of the most pristine and biodiverse rain forests on the planet, harboring an estimated 6,000 flowering plants (United Nations Environment Programme World Conservation Monitoring Centre, 2002; Hammond, 2005). More than 1,000 of these are used to treat a wide variety of diseases including diabetes mellitus (Havinga and Van Andel, 2008). Unfortunately, there is in many cases no hard scientific evidence to support the claims of clinical efficacy of these ethnopharmacological therapies.

For this reason, we decided to compile the most commonly recommended Surinamese plants for treating diabetes mellitus, and to evaluate them for their potential anti-diabetic efficacy on the basis of preclinical and clinical observations reported in the scientific literature. The information obtained is used to judge whether the plants and/or some of their products (crude extracts or isolated active principles) may be useful as oral hypoglycemic substances.

Materials and methods

Information about the plants and plant parts used in Suriname for treating diabetes mellitus has been acquired from a number of well-known publications on medicinal plants in the country. Scientific evidence of preclinical and/or clinical anti-diabetic activity of the plants has been obtained from scientific reports downloaded via the Internet from on-line electronic libraries. These literature sources provided also data about the chemical and/or pharmacological properties of biologically active plant substances and the possible mechanisms of action. The desired information was extracted using combinations of key words such as ‘scientific plant name - diabetes mellitus’, ‘scientific plant name - phytochemical composition’, ‘chemical composition - diabetes mellitus’, and ‘chemical composition - mechanism of action’.

Results

The most frequently recommended Surinamese medicinal plants against the symptoms of diabetes mellitus were compiled from the publications of May (1982), Titjari (1985), Tirimana (1987), Sedoc (1992), Raghoenandan (1994), and Heyde (1999). Together, these reports contain botanical, ethnopharmacological, as well as phytochemical data about more than 500 Surinamese medicinal plants. Based on this information, the fifteen most popular plants against diabetes mellitus in the country were found to comprise the neem Azadirachta indica, the dwarf periwinkle (kotomisi) Catharanthus roseus, the beggarweed (toriman) Desmodium canum, the mango (manya) Mangifera indica, the bitter melon (busi sopropo) Momordica charantia, the noni (didibri apra) Morinda citrifolia, the cat’s whiskers (kattesnor) Orthosiphon stamineus, the stonebreaker (finibita) Phyllanthus niruri, the wild tomato (batotobita) Physalis angulata, the amargo (kwasibita) Quassia amara, the mimnie root (watrakanu) Ruelia tuberosa, the ambarella (pomme citère) Spondias dulcis, the Jamaican vervain (isriwiwiri) Stachytarpheta jamaicensis, the jambolan (dyamun) Syzygium cumini, and the gros bouton (sukrutanta) Wulffia baccata (Table 1).

Figure 1: The dwarf periwinkle (kotomisi) Catharanthus roseus
Consulting peer-reviewed scientific articles, these plants were subsequently, assessed for preclinical and/or clinical evidence for activity against certain aspects or the symptoms of diabetes mellitus; suggestions about the mechanisms involved in these actions; and indications about the allegedly biologically active plant substances. The scientific articles were for the greater part retrieved from the academic libraries PubMed and Hinari.

As shown in Table 2, only four of the fifteen plants \((A. \text{ indica}, \text{ P. niruri, M. charantia, and S. cumini})\) had undergone preclinical as well as clinical evaluation against diabetes mellitus, and turned out positive in at

Table 1. Most frequently recommended plants against diabetes mellitus in Suriname.

<table>
<thead>
<tr>
<th>Plant species (popular name in English, Surinamese)</th>
<th>Family</th>
<th>Plant part (s) used</th>
<th>Reference (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{Azadirachta indica} A. Juss. (neem, nim)</td>
<td>Meliaceae</td>
<td>Leaves</td>
<td>Raghoenandan, 1994</td>
</tr>
<tr>
<td>\textit{Catharanthus roseus} L. (dwarf periwinkle, kotomisi)</td>
<td>Apocynaceae</td>
<td>Whole plant; roots; leaves and flowers</td>
<td>May, 1982; Titjari, 1985; Sedoc, 1992; Raghoenandan, 1994; Heyde, 1999</td>
</tr>
<tr>
<td>\textit{Desmodium canum} (J.F. Gmel.) Sch. &amp; Thell. (beggarweed, toriman)</td>
<td>Fabaceae</td>
<td>Roots</td>
<td>Raghoenandan, 1994</td>
</tr>
<tr>
<td>\textit{Mangifera indica} L. (mango, manya)</td>
<td>Anacardiaceae</td>
<td>Leaves</td>
<td>Raghoenandan, 1994</td>
</tr>
<tr>
<td>\textit{Momordica charantia} L. (bitter melon, busi sopropo)</td>
<td>Cucurbitaceae</td>
<td>Twigs and leaves</td>
<td>Raghoenandan, 1994; Titjari, 1987</td>
</tr>
<tr>
<td>\textit{Morinda citrifolia} L. (noni, didibri apra)</td>
<td>Rubiaceae</td>
<td>Leaves</td>
<td>Titjari, 1985; Sedoc, 1992</td>
</tr>
<tr>
<td>\textit{Orthosiphon stamineus} Bold. (cat’s whiskers, kattesnor)</td>
<td>Lamiaceae</td>
<td>Leaves</td>
<td>Titjari, 1985; Titjari, 1987</td>
</tr>
<tr>
<td>\textit{Physalis angulata} L. (wild tomato, batotobita)</td>
<td>Solanaceae</td>
<td>Whole plant</td>
<td>Heyde, 1999</td>
</tr>
<tr>
<td>\textit{Quassia amara} L. (amargo, kwasibita)</td>
<td>Simaroubaceae</td>
<td>Stems</td>
<td>Raghoenandan, 1994</td>
</tr>
<tr>
<td>\textit{Spondias dulcis} L. (ambarella, pomme citère)</td>
<td>Anacardiaceae</td>
<td>Fruits</td>
<td>Titjari, 1985; Sedoc, 1992</td>
</tr>
<tr>
<td>\textit{Stachytarpheta jamaicensis} (L.) Vahl (Jamaican vervain, isriwiswiri)</td>
<td>Verbenaceae</td>
<td>Leaves</td>
<td>Raghoenandan, 1994; Heyde, 1999</td>
</tr>
<tr>
<td>\textit{Syzygium cumini} L Skeels (jambolan, dyamun)</td>
<td>Myrtaceae</td>
<td>Seeds; bark; leaves; flowers</td>
<td>May, 1982; Titjari, 1985; Sedoc, 1992; Raghoenandan, 1994; Heyde, 1999</td>
</tr>
<tr>
<td>\textit{Wulffia baccata} (L.f.) O. Kuntze (gros bouton, sukrutanta)</td>
<td>Asteraceae</td>
<td>Leaves</td>
<td>Sedoc, 1992; Raghoenandan, 1994</td>
</tr>
</tbody>
</table>
Table 2. Indications about preclinical activity, clinical activity, mechanism(s) of action, and/or pharmacologically active principle(s)

<table>
<thead>
<tr>
<th>Plant species (popular name in English, Surinamese)</th>
<th>Preclinical activity</th>
<th>Clinical activity</th>
<th>Suggestions about bioactive principle(s)</th>
<th>Suggestions about mechanism(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>A. indica</em> (neem, nim)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td><em>M. charantia</em> (bitter melon, busi sopropo)</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>P. niruri</em> (stonebreaker, finibita)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>S. cumini</em> (jambolan, dyaman)</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>C. roseus</em> (dwarf periwinkle, kotomisi)</td>
<td>+</td>
<td>Not done</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td><em>M. indica</em> (mango, manya)</td>
<td>+</td>
<td>Not done</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>M. citrifolia</em> (noni, didibri apra)</td>
<td>+</td>
<td>Not done</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>O. stamineus</em> (cat’s whiskers, kattesnor)</td>
<td>+</td>
<td>Not done</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td><em>D. canum</em> (beggarweed, toriman)</td>
<td>Not done</td>
<td>Not done</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>P. angulata</em> (wild tomato, batotobita)</td>
<td>Not done</td>
<td>Not done</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>Quassia amara</em> (amargo, kwasibita)</td>
<td>Not done</td>
<td>Not done</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><em>R. tuberosa</em> (minnie root, watrakanu)</td>
<td>Not done</td>
<td>Not done</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>S. dulcis</em> (ambarella, pomme citère)</td>
<td>Not done</td>
<td>Not done</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>S. jamaicensis</em> (Jamaican vervain, isriwiwiri)</td>
<td>Not done</td>
<td>Not done</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>W. baccata</em> (gros bouton, sukrutanta)</td>
<td>Not done</td>
<td>Not done</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

At least some of the clinical studies. Four other plants (*C. roseus, M. indica, M. charantia, and O. stamineus*) have only been tested in preclinical models of diabetes mellitus. However, almost half of the plants (*D. canum, P. angulata, Q. amara, R. tuberosa, S. dulcis, S. jamaicensis, and W. baccata*) has never been assessed for potential anti-diabetic efficacy, not even in preclinical models (Table 2). Suggestions and indications about the chemical substances and/or the mechanisms involved in the apparent hypoglycemic actions were provided for seven plants (*A. indica, M. charantia, P. niruri, S. cumini, M. indica, M. citrifolia, and Quassia amara*; Table 2).

**Discussion**

*A. indica, C. roseus, D. canum, M. indica, M. charantia, M. citrifolia, O. stamineus, P. niruri, P. angulata, Q. amara, R. tuberosa, S. dulcis, S. jamaicensis, S. cumini, and W. baccata* are among the most widely used plants against the symptoms of diabetes mellitus in Suriname. However, a search in the scientific literature for evidence for their alleged anti-diabetic properties provided at the most some support for only a few cases.

Among the latter were *A. indica, P. niruri, M. charantia, and S. cumini*. Lipophilic, methanolic, or aqueous extracts of *A. indica* leaves or seeds caused a
clear decrease in (postprandial) blood sugar levels in streptozotocin- or alloxan-treated rabbits, rats, or mice (Chattopadhyay, 1996, 1999; Khosla et al., 2000; Kar et al., 2003; Akinola et al., 2010; Dholi et al., 2011; Rao et al., 2012). Such results were also found with methanol or aqueous extracts of *P. niruri* leaves or seeds (Raphael et al., 2002; Adeneye et al., 2006; Okoli et al., 2010) and aqueous extracts of *M. charantia* leaves (Lolitkar and Rao, 1962). An extract from the water-soluble gummy fibres of *S. cumini* seeds, the ethanol extract of powdered *S. cumini* seeds, and a purified fraction of *S. cumini* seeds elicited also meaningful hypoglycemic effects in alloxan- and streptozotocin-induced diabetic rats and mice (Pandey and Khan, 2002; Singh and Gupta, 2007; Dusane and Joshi, 2011). However, a tea from the leaves of this plant remained without effect on postprandial blood glucose levels in streptozotocin-treated rats (Teixeira et al., 1997, 2000).

The actions of the *M. charantia* extract were ascribed to charantine, a mixture of steroid saponins (Lolitkar and Rao, 1962), and/or to certain lectins (Raman and Lau, 1996). That of the *P. niruri* preparations might be mediated by lignans such as phyllanthine and hypophyllanthine, certain alkaloids, and/or bioflavonoids such as quercetine (Sharma et al., 1993; Somanabandhu et al., 1993). And that of the *S. cumini* seeds could be attributable to ferulic acid (Mandal et al., 2008), a phenolic compound found abundantly in the plant kingdom and reported to lower blood sugar levels in type 2 diabetic mice (Jung et al., 2007).

The mechanisms associated with the apparent hypoglycemic actions of the plants might involve stimulation of insulin release by the β cells (Visarata and Ungsurungsie, 1981; Raman and Lau, 1996; Virdi et al., 2003; Shetty et al., 2005; Sridhar et al., 2008), stimulation of glucose uptake by the peripheral tissues (Visarata and Ungsurungsie, 1981; Chattopadhyay, 1996, 1999; Raman and Lau, 1996; Virdi et al., 2003; Shetty et al., 2005; Adeneye et al., 2006; Sridhar et al., 2008), inhibition of glycogenolysis in the liver (Chattopadhyay, 1996, 1999), inhibition of glucose absorption and enhancement of glucose storage (Okoli et al., 2011), and/or inhibition of α-glucosidase activity in the duodenum followed by slowing down of carbohydrate digestion and glucose resorption (Shinde et al., 2008; Bhat et al., 2009).

In clinical studies, dried aqueous and alcoholic extracts of *A. indica* seeds were observed to lower blood sugar levels considerably in treatment-naïve patients with type 2 diabetes mellitus as well as in patients who responded poorly to conventional hypoglycemic therapy (Waheed et al., 2006). *P. niruri* extracts produced comparable results (Sivaprakasam et al., 1995; Sridvidy and Periwal, 1995), although patients with non-insulin-dependent diabetes mellitus did not respond to the extract (Moshi et al., 2001). One clinical study (Lim et al., 2010) with the leaf extracts from *M. charantia* also confirmed the preclinical findings. However, this was contradicted by the results from other clinical trials (for instance, Dans et al., 2007; Ooi et al., 2010). Preparations from the leaves of *S. cumini* also did not pass clinical evaluation (Teixeira et al., 2004; Teixeira et al., 2006). However, reviewing historical literature dating back to the pre-insulin era, as well as more recent in vitro, animal, and in vivo studies (Helmstädt, 2008), it was concluded that a successful clinical study should use *S. cumini* seeds, seed kernels, or fruit in fairly high doses rather than extracts from the leaves of this plant.

Experimental evidence for a possible blood sugar-lowering activity of *C. roseus*, *M. indica*, *M. citrifolia*, and *O. stamineus* is so far limited to a handful of preclinical studies. Extracts from *C. roseus* flowers and/or leaves (Chattopadhyay et al., 1991; Ghosh and Suryawanshi, 2001; Kar et al., 2003), *M. indica* leaves (Aderibigbe et al., 1999, 2001), *M. citrifolia* leaves, fruits, or roots (Nayak et al., 2007; Kamiya et al., 2008; Horsfall, 2008), and *O. stamineus* leaves (Sriplang et al., 2007) decreased blood sugar levels in diabetic mice or rats.

The *C. roseus* extracts were found to promote repair of the pathological changes in the islets of Langerhans (Ghosh and Suryawanshi, 2001), those from *M. indica* to reduce intestinal resorption of glucose (Aderibigbe et al., 1999), those from *M. citrifolia* – containing anthracinones as potentially active ingredients (Kamiya et al., 2008) – to accelerate wound healing (Nayak et al., 2007) and to act synergistically with insulin (Horsfall, 2008), and those from *O. stamineus* to decrease plasma triglyceride concentrations (Sriplang et al., 2007). Of note, the xanthone glycoside mangiferin - the pharmacologically active principle in *M. indica* leaves - elicited a marked hypoglycemic effect in diabetic rats.
(Muruganandan et al., 2005), and prevented progression of diabetic nephropathy and renal damage in a diabetic nephropathy rat model and cultured rat mesangial cells (Li et al., 2010).

Thus far, there are no experimental data available about a possible hypoglycemic activity of preparations from D. canum, P. angulata, Q. amara, R. tuberosa, S. dulcis, S. jamaiicensis, and W. baccata. However, Q. amara extracts have also been reported to contain phyllanthin and hypophyllanthin (Mentreddy, 2007), the lignans implicated in the hypoglycemic actions of P. niruri. Furthermore, an extract from the seeds of the Q. amara family member Brucea javanica (L.) Merr. caused a significant decrease in blood sugar levels in streptozotocin-treated rats, presumably by stimulating insulin release by quassinoids such as bruceins (NoorShahida et al., 2009).

Summarizing, the data from this survey indicate that the scientific evidence accumulated so far to support the use of plant-based traditional medicines in Suriname against diabetes mellitus is scant. Preparations from A. indica and P. niruri may elicit blood sugar-lowering effects in diabetic patients, but these assumptions are based on the results from relatively few clinical studies. Those from M. charantia have been found positive in some clinical studies but negative in others, and those from S. cumini – at least S. cumini leaves – were negative. The preparations from C. roseus, M. indica, M. citrifolia, and O. stamineus have only undergone preclinical testing, while those from D. canum, P. angulata, Q. amara, R. tuberosa, S. dulcis, S. jamaiicensis, and W. baccata have not even gone through such evaluations. These findings raise not only the possibility that diabetic patients treat their disease with substances that may be ineffective, but that they may also run the risk of unknown or unforeseen adverse effects. For these reasons, it is necessary to subject these plants to well-designed and well-executed clinical studies to definitely establish their roles in the treatment of diabetes mellitus.

References


