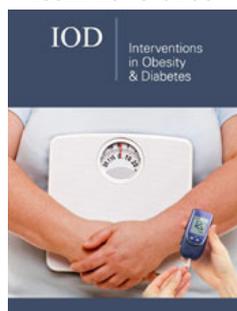


# Anti-Diabetic Plants Used in Cameroon with a Potential of Endogenous Renewal Pancreatic $\beta$ -Cells Important in the Management of Diabetes

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## Abstract

Type 1-diabetes is the result of pancreatic  $\beta$  cells autoimmune destruction, whereas Type 2-diabetes is the result of the mixture of insulin resistance and inadequate insulin excretion. Thus, for both diabetes types, the functional mass of  $\beta$  cells is not enough for the control of blood glucose. These two pathologies touch approximately 200 million people worldwide today. Type 2-diabetes is globally a huge economic problem. According to the International Diabetes Foundation 382 million people were diagnosed with diabetes in 2013 and this number is expected to increase to 592 million by 2035. Beta-cell regeneration is a natural procedure that produces new beta cells, which synthesize and discharge insulin in the pancreas. Users of plants like local therapists are interested in taking advantage of these mechanisms to select plant species for preventing, treating or curing diabetes. **Objective and methods:** The purpose of the present article is to identify from medicinal plant species published by Cameroonians those with the potential to renew the pancreatic  $\beta$ -cells mass, through bibliographic research in Google, PubMed, Google Scholar databases. **Results:** Over 210 plants are reported to have antidiabetic effects in Cameroon. About 12 plants among them have been confirmed as antidiabetic plants. Among other plants used for the treatment of diverse diseases 6 have beta cells regeneration activity. However, few clinical trials have evaluated the effectiveness and safety of these plants. Many studies have shown that 9 plants presented pancreatic beta cells regeneration outcomes. Amongst them, *Bidens pilosa* exerted antidiabetic action via the regulation of  $\beta$ -cell function. *Annona muricata* have reduced oxidative stress of pancreatic  $\beta$ -cells of streptozotocin induced diabetic rats by increasing the  $\beta$ -cells number. Alcoholic extracts of whole *Catharanthus roseus* plant has been released diabetes through  $\beta$  cell regeneration. **Conclusion:** Modern clinical evaluations of recorded ethnopharmacological medicine will be investigated to estimate their efficacy and safety in humans and then use them to prepare herbal medicines worldwide.

**Keywords:** Anti-diabetic plants; Potential antihyperglycemic plants; Bioactive antidiabetic compounds; Pancreatic beta cells regeneration; Cameroon

## Introduction

### Diabetes and late healthcare in developing countries

Diabetes is a chronic metabolic, genetic and environmental worldwide disease characterized by hyperglycemia. This high blood glucose concentration is due to insufficient synthesis of endogenous insulin by the pancreas beta cells for the type-1 diabetes, or impaired insulin production and/or activity for type-2 diabetes [1]. So type-1 diabetes is an autoimmune disease due to the destruction of T-cell mediated located in the pancreas beta cells. Yet type-2 diabetes is characterized by a development of insulin resistance and beta cell dysfunction. These two metabolic disorders are strongly associated with obesity and a sedentary lifestyle [2,3]. In many developing countries diabetes was considered as a disease of wealth countries. That is why three decades ago, undiagnosed diabetic patients perished, killed by this insipid and complicated pathology [4,5]. Face to this undesirable situation many scientific, administrative and social efforts were done in Cameroon to combat diabetes. The recrudescence of the prevalence of diabetes, especially amongst towns' dwellers, the over expensive cost and the long duration of treatment oblige Cameroonians through local therapists to utilize medicinal plants to fight this symptomatic disease. The plants used were selected amongst medicinal plants which were used from centuries for the treatment of various human ailments. Herbal preparations because of its cost effective, safety and substitution for the treatment of diseases are also strongly used for diabetes mellitus [6]. The purpose of the present article is to identify from medicinal plants published by Cameroonians those which

are potential renewal of pancreatic  $\beta$ -cells, through bibliographic research in Google, PubMed, Google Scholar databases. Responses to the following research questions are needed to better understand the function of pancreatic beta cells in the treatment of diabetes. What are beta cells? Where are they located? What is their role in the processes of hyperglycemia regulation? What is the cause of their destruction? Are plants able to regenerate them? The commentary below clearly provides answers to these questions in a succinct and precise manner.

**Location of pancreas**

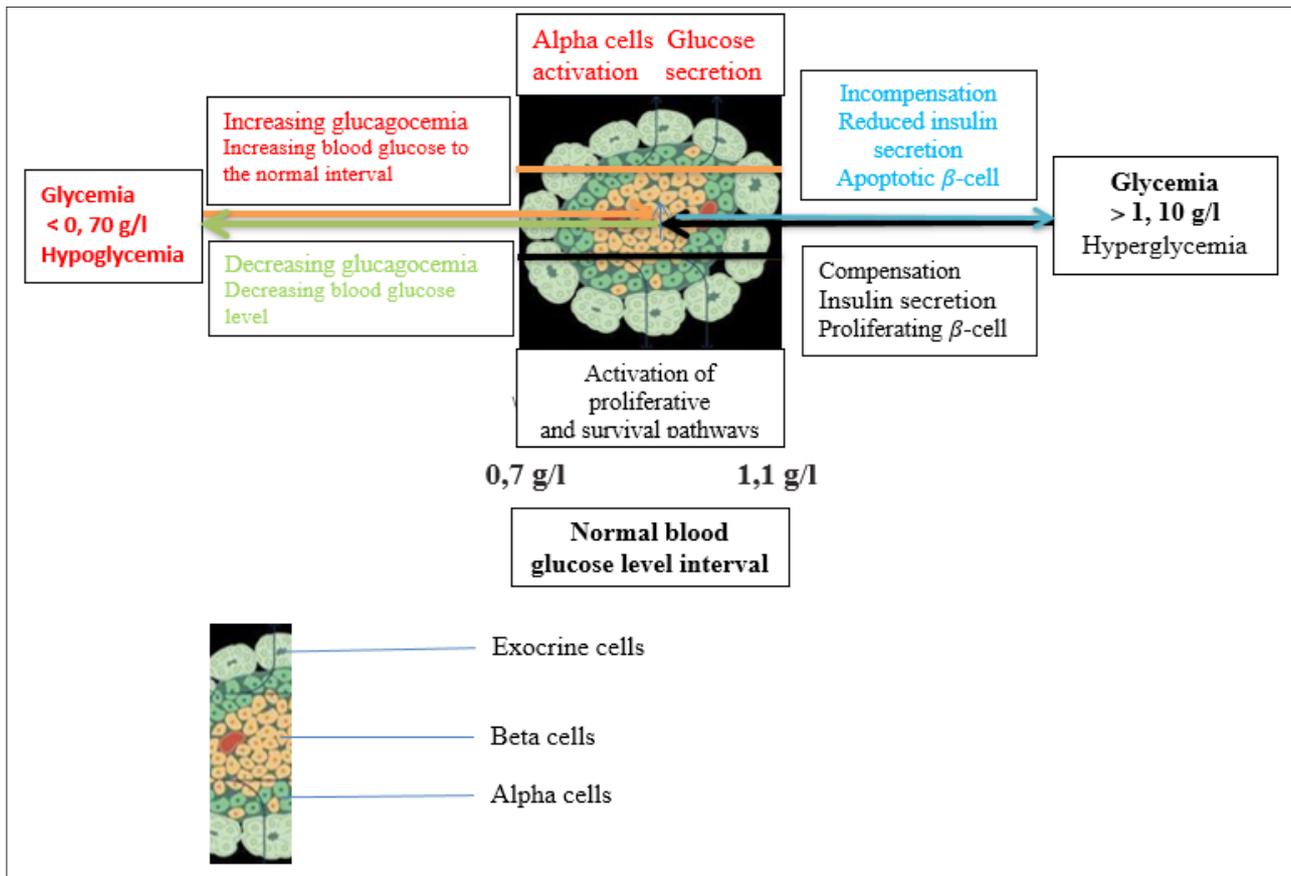
The pancreas is a glucose controlling organ, located below stomach and before small intestine in the middle of duodenum. The beta cells which secrete insulin are located in this organ.

**Exocrine and endocrine functions**

The pancreas is a complex organ exercising exocrine and endocrine functions. The exocrine pancreas is made up of acinar

cells that produce and secrete digestion enzymes that will be transported to the intestine through the pancreatic duct system. The endocrine pancreas, which controls glucose homeostasis, is organized into micro-organs (the islets of Langerhans), dispersed throughout the pancreatic tissue and composed of five cell types,  $\alpha$ ,  $\beta$ ,  $\delta$ ,  $\epsilon$  and PP respectively secreting glucagon, insulin, somatostatin, ghrelin and the pancreatic polypeptide. Insulin-secreting cells being by far the most numerous, following by  $\alpha$  cells.

A closer look at the islets of Langerhans reveals that these contain 2 principal types of cells:  $\alpha$  cells at the periphery and  $\beta$  cells at the center. The pancreas secretes two hormones: insulin and glucagon. Insulin is produced by  $\beta$  cells and glucagon is made by  $\alpha$  cells. As the islets of Langerhans are richly vascularized, these cells directly release hormones into the blood. The pancreas therefore has a double function: the secretion of digestive enzymes and the production of hormones released in the blood allowing the regulation of blood glucose (Figure 1).



**Figure 1:** Glycaemia pancreatic regulation.

**Insulin is a blood sugar lowering hormone**

$\beta$  cells are directly sensitive to blood sugar. The higher the blood sugar, the more insulin released. Blood insulin works on cells using specific protein receptors in their plasma membranes: these are target cells. Insulin does not enter these cells. Insulin acts on a

very large number of target cells:

- a. liver cells,
- b. muscle cells,
- c. adipose tissue cells (adipocytes),

- d. more other organs, except cells of the nervous system.
- e. insulin has several roles:
- f. promote the penetration of glucose into the liver;
- g. favor its use in cellular respiration in the muscles,
- h. stimulates glycogen genesis and inhibits glycogenolysis (storage of glucose in the form of increased glycogen in the liver),
- i. stimulates lipogenesis from glucose and inhibits the hydrolysis of fats. In general, insulin therefore promotes the storage of glucose and its use; it therefore lowers the level of glucose in the blood. It is a hypoglycemic hormone. It is the only hypoglycemic hormone the body has (Figure 1).

### Glucagon: A hyperglycemic hormone

The cells secrete glucagon (polypeptides of 29 amino acids). They lower the blood sugar. Glucagon also binds to specific receptors on the membranes of these target cells, which are only liver cells. Glucagon increases blood sugar; it is a hyperglycemic hormone. Glucagon works by stimulating glycogenolysis, increased release of glucose into the blood. The body has other hyperglycemic hormones like adrenaline, cortisol... (Figure 1).

### Insulin and glucagon are antagonistic hormones

When the blood sugar is between 0,7g/L and 1,1g.L<sup>-1</sup>, the secretions of insulin and glucagon are low: this is called basal secretions. If the blood sugar raises, the insulin level increases, the glucagon level decreases, the insulin/glucagon ratio becomes very high, and glucose is stored. If the blood sugar goes down, it's the inverse that will produce (Figure 1).

### Antidiabetic bioactive compounds

This work aims to research bioactive compounds responsible of plant pancreatic beta cells regeneration and regulation of oxidative stress.

### Pancreatic beta regeneration of bioactive compounds

These substances are effective in the treatment of type 1-diabetes, by stimulating the beta cells production and insulin releasing by these special cells. More an antidiabetic plant has a strong number or concentration of these compounds more the plant can potentially stimulate the synthesis of beta cells.

### Antioxidative stress active compounds

Compounds of this group can act as an effective insulin sensitizing and insulinotropic agent. That means antioxidative stress substances increase glucose-stimulated insulin secretion.

### Importance of ethnopharmacology

As manifold conventional antihyperglycemic drugs many antidiabetic plants are used in Cameroon, but diabetes still a health problem. Numerous local therapists do not pose correct diabetic diagnostic and its complications. They do not know well the strong variety of natural hypoglycemic substances found in ethnomedical

medicines, used widely in African, South American, and Asian traditional medicine for diabetes management. Therefore the identification of plants or antidiabetic compounds with pancreatic beta cells regeneration will help them to use appropriate herbal medicines for type 1-diabetes. As a result of over-nutrition and progressively inactive lifestyles, type 2 Diabetes has reached epidemic proportions. Modern therapies, while effective, are restricted. These restrictions, the frightening upsurge in the prevalence of diabetes, and the climbing cost of managing diabetes and its complications emphasizes an urgent need for innocuous, more efficient and affordable alternative treatments [7]. Some bioactive plants extracts and isolated compounds such as, beta-pyrazol-1-ylalanine, cellobioside, cinchonain Ib, christinin-A, dehydrotrametenolic acid, epicatechin, epigallocatechin gallateleucocyanidin 3-O-beta-d-galactosyl leucopelargonidin-3-O-alpha-L rhamnoside, glycyrrhetic acid, roseoside strictinin, isostrictinin, pedunculagin, show significant insulinomimetic and antidiabetic activity with more efficacy than conventional hypoglycaemic agents [8]. Insulin therapy has been assessed with significance to enhancement in inflammatory conditions but the defect in the anti-aging gene Sirt 1 and diabetic mitophagy still persists with the introduction of nonalcoholic fatty liver disease and various organ diseases [9]. Therefore recorded species can be highlighted by their possible integration into the healthcare system.

## Materials and Methods

### Criteria of plants inclusion

Plants admitted in this work must be used in Cameroon and reencountered in publications authorized by Cameroonians on diabetes. Plants for the management of type 1-diabetes were more indorsed. Extracts of these plants or compounds isolated from them showed diverse antihyperglycemic activities especially in type 1-diabetes. The review was performed in Google, Google Scholar and Pubmed since five years.

### Ethno pharmacological doses

Standardized doses of recipes were calculated by deduction from experimental doses used to treat *in vivo* alloxan-induced or streptozotocin-induced diabetic rats or diabetic patients in cases of clinical trials. For example a patient of 60kg body weight would take 60 times the quantity of abstracts administrated for a kilogram body weight of experimental animals. Generally the dose is related to the weight of a given person.

### Authentication of plants identification

Plants taxonomical accepted names or their synonyms were searched in African Plants database.

## Results

Over 210 plants were supposed to have antihyperglycemic properties in Cameroon [10-30]. About 13 plants among them have been confirmed as antidiabetic plants [10-30]. Among other plants used for the treatment of diverse diseases 6 have beta

cells regeneration activity. However, few clinical trials have ever evaluated the effectiveness and safety of these plants [26,29]. Many studies have shown that 9 plants presented pancreatic beta cells regeneration. Amongst them *Bidens pilosa* exerted antidiabetic action via the regulation of  $\beta$ -cell function [31-35], *Annona muricata* have reduced oxidative stress of pancreatic  $\beta$ -cells of

streptozotocin induced diabetic rats by increasing the number of insulin immunoreactive  $\beta$ -cells and their protection against degeneration. In this review 9 plants were admitted. They belonged to Cameroonians' publications on diabetes randomized selected in all regions. Their strategy to regenerate pancreatic beta cells [36-55], significant to manage diabetes is presented in Table 1.

**Table 1 :** Existing pancreatic beta cell regeneration' mechanisms of antidiabetic plants commonly used in Cameroon effects. SNPAPRP: Scientific names of potential antidiabetic plants and references of their publications; PPSERPBC: Pharmacological previous scientific evidence of the regeneration of pancreatic beta cell by each plant recorded; PEPPEU: Experimental doses of plants' extracts or isolated; PPCDED: Proposed posology calculated by deduction from the experimental doses used to treat *in vivo* alloxan-induced or streptozotocin-induced diabetic rats or diabetic patients in case of clinical trials.

SNPAPRP	Common and Vernacular Names	PPSERPBC	PEPPEU and PPCDED
<i>Annona muricata</i> Lin. ( <i>Annonaceae</i> )	Corrossol, guanabana, soursop	<i>Annona muricata</i> have reduced oxidative stress of pancreatic $\beta$ -cells of streptozotocin induced diabetic rats. This reduction was confirmed by the increased number of insulin immunoreactive $\beta$ -cells and their protection against degeneration [36].	50, 100 and 200mg/kg body weight
<i>Bidens pilosa</i> Lin. ( <i>Asteraceae</i> )	Blackjack, cobbler's pegs, hairy beggarticks, Spanish needles (English). Sornet, piquant noir, bident hérissé, herbe aiguille, herbe villebague (French).	The research of Lai et al. showed that treatment of diabetic patients with a <i>Bidens pilosa</i> formulation (400mg/day) for three months decreased fasting blood glucose concentration and hemoglobin A1c (HbA1c), but augmented fasting serum insulin in healthy subjects [35]. Treatment with the <i>Bidens pilosa</i> formulation significantly improved pancreatic beta cell function of the study members compared with homeostatic model assessment beta (HOMA- $\beta$ ) values. Consequently, <i>Bidens pilosa</i> or its active compound derivatives cytopiloyne could be potential mediators to manage type 2 diabetes by stimulating pancreatic beta cells [36].	(400mg/day) body weight for three months
<i>Catharanthus roseus</i> Lin. ( <i>Apocynaceae</i> )	Pervenche de Madagascar, rose amère (French). Vinca, Madagascar periwinkle, rosy periwinkle (English).	The administration of alloxan in rats to induce diabetes provokes hyperglycemia by increasing the blood glucose level during seven days experimental period. The treatment by <i>Catharanthus roseus</i> has decreased the level of glucose in diabetic rats. The number of $\beta$ cell increased despite its destruction. It was concluded that regeneration of pancreatic $\beta$ cells following destruction by alloxan may be the primary cause of the lowering of hyperglycemia [37]. Therefore alcoholic extracts whole <i>Catharanthus roseus</i> plant has been released diabetes through $\beta$ cell regeneration [38].	250mg/kg body weight.
<i>Capsicum annum</i> Lin. ( <i>Solanaceae</i> )	Chili pepper, Aromatic pepper Piment, Poivron	<i>Capsicum annum</i> is a spice plant with fruit rich in the major compound called Capsaicin [39]. Administration of capsaicin to Zucker diabetic fatty streptozotocin-induced (ZDF) rats decreased blood glucose concentrations and augmented plasma insulin levels compared with those of switch mice [40]. Capsaicin in dietary supplementation of red fruits powder for two weeks to this treated rats nourished a high-fat diet did not lower the blood glucose concentration, but the plasma insulin level was greater in these rats than that in the control group, signifying that capsaicin holds an insulintropic effect rather than hypoglycemic upshot [39,41]. But clinical trial is needed to determine its mechanism in diabetic patients.	150 or 300mg/kg body weight
<i>Carica papaya</i> Lin. ( <i>Caricaceae</i> )	papayer, "pied-papaye" Papaya	<i>Carica papaya</i> leaves show antidiabetic activity and bioactive phytochemicals are speculated to be Flavonoids, alkaloids, saponins, and tannins. The leaves (0.75g 1.5g/100mL) aqueous extract of <i>Carica papaya</i> significantly decreased plasma blood glucose concentration, serum cholesterol, and serum triacylglycerol in streptozotocin-induced and alloxan-induced diabetic rats [41]. Histological discoloration of the pancreatic islets of Langerhans presented that these extracts significantly decreased the regeneration of pancreatic beta cells [42,43]. Future research is required for elucidating the antidiabetic effect of <i>Carica papaya</i> in humans.	0.75g 1.5g/100mL) aqueous extract

<p><i>Camellia sinensis</i> (Theaceae)  <i>Coffea arabica</i> Lin. and <i>Coffea canephora</i> Pierre  Syn. <i>C. robusta</i> Lindl. Ex De Will) (<i>Rubiaceae</i>)</p>	<p>Thé vert, Théier (French), Tea, green tea (English).  <i>Café arabica</i>. <i>Caféier</i> (French), Robusta coffee (French)</p>	<p>Caffeine is anti-diabetic bioactive compound isolated from <i>Camellia sinensis</i>, <i>Coffea arabica</i> and <i>Coffea robusta</i>. So it has been demonstrated that the treatment with 0.01% caffeine solution in 90% pancreatectomized diabetic rats for 12-week decreased body weight, fats, and lowered insulin resistance and boosted glucose-stimulated insulin secretion and beta-cell hyperplasia [44].</p>	<p>100mg/kg body weight/day  63 and 93mg/kg body weight</p>
<p><i>Elephantopus scaber</i> Lin. (<i>Asteraceae</i>)</p>	<p>Elephant's Foot</p>	<p>The acetone extract of this plant showed a significant reduction in blood glucose concentration by increasing insulin sensitivity, augmenting glucose dependent insulin secretion and stimulating regeneration of beta cells in islets of Langerhans in pancreas of streptozotocin-induced diabetic rats [45].</p>	<p>Leaf extracts (0.3g/kg body weight) for 12 weeks</p>
<p><i>Momordica charantia</i> Lin. (<i>Curcubitaceae</i>)</p>	<p>bitter guard, karela, or balsam pear</p>	<p>Diabetes treatment with a water extract of <i>Momordica charantia</i> prevented alloxan-induced pancreatic beta cell apoptosis and improved insulin emission in HIT-T15 cells [46]. The treatment with fruit juice of this plant showed a significant reduction of blood glucose level and increased rate of plasma insulin in diabetic rats. The observed actions were outstanding to an upsurge in the number of beta pancreatic cells in cured animals compared to untreated one. The principal phytochemical such as momordicin, charantin, and other compounds such as galactose-binding lectin and insulin-like protein found in several parts of this plant have been revealed insulin mimetic effect [47,48].  <i>Momordica charantia</i> increases the renewal of some cells in the pancreas or may permit the recovery of partially destroyed cells and stimulates pancreatic insulin discharge [49].</p>	<p>0.25, 0.50 and 0.75mg/kg body weight</p>
<p><i>Moringa oleifera</i> Lam. synonym: <i>Moringa pterygosperma</i> Gaertner (<i>Moringaceae</i>)</p>	<p>Drumstick, horseradish tree (English); mouroungue, ben ailée, moringa ailée (Fr); maranga, paraíso</p>	<p>Two concentrations (150 and 300mg/kg body weight) of methanolic pods extract of <i>Moringa oleracea</i>, administered in streptozotocin-induced diabetic rats showed a significant decrease in serum glucose rate and nitric oxide levels, with a simultaneous upsurge in serum insulin and protein levels. Additionally, a histological pancreas examination showed that <i>Moringa oleifera</i> treatment significantly reversed the histopathological damage that occurred to islet cells by induced diabetes. The <i>Moringa oleifera</i> leaves consumption by alloxan-induced diabetic rats, showed a hypoglycemic/upshot and prevented body weight loss [50].</p>	<p>150 and 300mg/kg body weight</p>
<p><i>Persea americana</i> Lin. (<i>Lauraceae</i>)</p>	<p>Avocatier, avocat (French) Avocado, tree, Pear tree (English)</p>	<p>The hydroalcoholic leaves extract of <i>Persea americana</i> (0.15 and 0.3g/kg, body weight, daily for 4 weeks) decreased blood glucose concentration in streptozotocin-induced diabetic rats [51]. The extract did not modify the concentration of plasma insulin. This result suggests that the hypoglycemic effect was provoked by an extra pancreatic activity, autonomous of insulin excretion. Additionally, the extract enhanced the metabolic condition of diabetic rats and augmented body weight. In another study, the aqueous extract of <i>Persea americana</i> seeds meaningfully reduced glucose rates and reversed the histoarchitectural damage in alloxan-induced diabetic rats, comparable to the effects of glibenclamide (an oral antihyperglycemic) [52].</p>	<p>0.15 and 0.3g/kg body weight</p>
<p><i>Solanum torvum</i> Swartz (<i>Solanaceae</i>)</p>	<p>Turkey berry</p>	<p>At 200 and 400mg/kg phenolic compounds isolated from <i>Solanum torvum</i> fruit methanolic extract decreased blood glucose rates in streptozotocin induced diabetic rats in two principal ways:  1- augmenting insulin secretion due to regeneration of pancreatic <math>\beta</math>-cells,  2- weakening oxidative stress and regulate enzymes in charge for glucose metabolism [53].  Also Methyl caffeate, main principle found in the fruit of <i>Solanum torvum</i> at concentrations 10, 20 and 40mg/kg significantly decreased hyperglycemia activity in streptozotocin induced diabetic by up regulation of a protein from the class I transporter family, whose essential role is the transport of glucose (GLUT4) from plasma to muscle and adipose tissue and renewal of pancreatic <math>\beta</math>-cells in the pancreas [54].</p>	<p>100 and 400mg/kg/day, body weight</p>

<i>Terminalia catappa</i> Lin. ( <i>Combretaceae</i> ):	Indian almond, tropical almond, Singapore almond, country almond, Malabar almond, sea almond (English), badamier ; amandier-pays (Guadeloupe, Martinique), amandier des Indes (Haïti), amandier de Cayenne (Guyane) (French)	Three extracts of <i>Terminalia catappa</i> fruits including petroleum ether, methanol and aqueous extract administrated in alloxan-induced diabetic rats produced a significant antihyperglycemic effect at dose levels of 1/5 of their lethal doses. The reduction of blood glucose level may be due to pancreatic $\beta$ -cells regeneration [55].	aqueous extract 343, 195, and 210mg/kg, body weight
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## Discussion

Extracts of recorded plants and/or their bio actives compounds play an antidiabetic role by alleviating oxidative stress (*Annona muricata*, *Solanum torvum*), and  $\alpha$ -glucosidase activity, improving endothelial dysfunction, modulating cytokine expression diabetes-induced damages of neural cells (*Bidens pilosa*, *Carica papaya*, *Annona muricata*) and provoking, ameliorating insulin resistance, (*Momordica charantia*) suppressing hyperglycemia (*Persea Americana*, *Momordica charantia*), improving hyperglycemic complications (*Carica papaya*, *Moringa oleifera*), regulating signaling pathway involving in diabetes, enhancing immunity, alleviating pancreatic  $\beta$ -cells regeneration (*Elephantopus scaber*, *Momordica charantia*, *Solanum torvum* and *Terminalia catappa*). The antidiabetic effect of plants depends on the bioactive compounds in each plant. It is important to isolate purified individual bioactive compounds so as to test their antidiabetic effect individually. This will help to clarify the principal antidiabetic components in plants and be interesting for improvement of plant processing. The chemical composition of plants varies with the plant cultivars, the processing of compounds isolation and conservation, which lead to unpredictable antidiabetic results between various tests using plants from various habitats. Bioavailability is an important factor influencing the pharmaceutical effects of plants on diabetes [56]. Tea and its extract play all these antidiabetic roles. For these reasons the daily consumption of at least three cups of tea reduced the risk of type 2-diabetes by approximately 42% [57]. The major chemical constituents in unfermented tea are catechins and caffeine, while in semi-fermented and fully fermented tea theaflavins, thearubigins and caffeine preponderate. Catechins, caffeine and theaflavins have been long-established to hold a comprehensive range of biological actions [56,58]. Recorded plants with insulinomimetic activity include the following: *Camellia sinensis* and *Catharanthus roseus* [3]. The bioactive compounds from the antidiabetic plants described that have major effects on the pancreas and renew pancreatic beta cell mass are: Capsaicin in *Capsicum annum*; 3 polyynes or cytopiloyne derivatives in *Bidens pilosa* [35]; phenylpropanoid esters, flavonoids, quinate, quinic acid, coumarate, caffeate, naringenin and quercetin on synergistic action, isolated from *Carica papaya* [37]; Epigallocatechin-3-gallate in *Camellia sinensis*; Momordicin in *Momordica charantia*; Quercetin Commonly found in recorded plants [6]. Particularly the quercetin in *Moringa oleifera*

leaves has anti-diabetic property by correcting pancreatic beta-cells dysfunction and insulin resistance, thereby increasing insulin secretion.

All the recorded plants have been reported to either reduce blood glucose concentration or to protect pancreatic  $\beta$  cells in diabetic animals. In consequent the development of antidiabetic medicines from these plants and active substances may increasingly receiving attention. But the neurodegenerative diseases such as Parkinson's disease (PD) and Alzheimer's disease with appetite dysregulation, insulin resistance and cell apoptosis can complicate the management of diabetes [38].

## Conclusion

We can conclude that this work has presented a list of antidiabetic plants used in the traditional management of diabetes mellitus that specifically improved pancreatic beta cells regeneration. It disclosed that plants have antihyperglycemic activities and can be used against numerous types of secondary complications of diabetes mellitus. Many antidiabetic active compounds found on plants like *caffeine*, *momordicin*, charantin, and other compounds such as galactose-binding lectin and insulin-like protein, have been well characterized. More investigations must be carried out to evaluate the exact mechanism of action of antidiabetic plants and antihyperglycemic active ingredients. It is always believed that plant is safe, but so many plant materials are not safe for the humankind, that's why toxicity study of these plants should also be clarified before ingestion of these plant materials. But food plants may be less toxic. We can also conclude that sociocultural medicine and ethnopharmacology are a huge source of information on safety and medical effects of many recorded plants, used to treat hyperglycemia since early time. Indeed, derive from traditional uses, plants like *Coffea arabica*, *Coffea robusta*, *Carica papaya* and *Camellia sinensis* possess anti-diabetes activities, officially recognized in one or more world regions. These activities are reinforced by clinical proof and registered in WHO monographs. Therefore these plants must be used with minimum attention [54,55]. Nevertheless clinical trials in complex animals and human are required. Before that, these plants need to be bio cultivated far of towns' pollution to avoid xenobiotics [56]. Generally the plans to decrease exposure to xenobiotics are imperative to manage the epidemic for diabetes worldwide [56].

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