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Contribution to the Management of Abnormal Insulin Secretion in Diabetes of Pregnancy using Antidiabetic Medicinal Plants in Cameroon

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Abstract

Abnormal insulin secretion occurs during hypoinsulinism and hyperinsulinism. Hypoinsulinism is absolute or relative insulin insufficiency which produces a very common clinical sickness called diabetes mellitus. Hyperinsulinism designs an overhead normal level of insulin in a patient's blood. Hyperinsulinism is the disproportionate production of insulin by tumors of the pancreatic β cells. Patients who suffer from hyperinsulinism disorder undergo hypoglycemic crises, weakness, intense perspiring, and vertigo. This alteration is not known by people of surrounding areas of developing countries like Cameroon. To identify previous work used to write this article a systematical search was done using engines including: "Antidiabetic plants help to control the hyperinsulism in pregnant diabetic women or animals" and "Toxicity of a given recorded plant name" used to verify the harmlessness of recorded plants. Plants that caught our attention are plants already used by hinterlands diabetic women in Cameroon. An increase in insulin secretion by fetal pancreas and placenta coincides with an increased number of insulin-producing B-cells to lower glucose levels in the bloodstream and promote the storage of glucose in adipose and muscle tissue, liver and other body tissues. It was demonstrated that insulin released from the liver stimulate also glucose uptake and naturally maternal insulin does not cross the placenta. Well controlled healthy pregnant women have a good chance of having a normal pregnancy and birth. But in developing countries diabetes is not generally well controlled during pregnancy in many hinterland areas and still affecting maternal and baby health. At the time of birth newborns diabetic mothers are still often larger, and after birth their vagina is harder and may upsurge the risk for nerve injuries and other trauma during birth. Also many risk including birth defect of the lower spine, birth defect of the brain, and limb result from pre-existing diabetes. Screening of all pregnancy for insulin resistance and early intervention may help to reduce these connected complications. Do antidiabetic plants more economical and available, taken by indigenous gestational diabetics control GDM?

Keywords: Gestational Diabetes; Antidiabetic Activity; Herbal Medicines; Insulin Insensitivity; Previous Mechanisms of Action

Abbreviations: IDM: Infants of Diabetic Mothers; IGF: Insulin Growth Factor; GDM: Gestational Diabetes Mellitus; IR: Insulin Resistance; IRS-1: Insulin Receptor Substrate-1; HFD: High Fat Diet; CHI: Congenital Hyperinsulinism; PHHI: Persistent Hyperinsulinemic Hypoglycemia of Infancy; IV: Intravenous; ICU: Intensive Care Unit; NICU: Neonatal ICU; MTD: Maximum Tolerated Dose; SREBP1c: Sterol-regulatory-element-binding protein 1c, a transcription factor; Fas: The Fas receptor, also known as Fas, FasR, apoptosis antigen 1; The Fas receptor is a death receptor on the surface of cells that leads to programmed cell death (apoptosis); HF: High fat; MTD : Maximum tolerated dose

Introduction

Normal insulin secretion and blood concentrations are closely connected to the level of sugar in the blood, so that a given level of insulin can be normal for one blood sugar level but low or high for another. Gestational diabetes mellitus is a disorder characterized by hormones produced by the placenta and by the fetus, which inhibit the body from using insulin fruitfully and it naturally resolves after the birth. It occurs during pregnancy and increases insulin resistance that prevent the body from using insulin successfully. Consequently, glucose stocks in the mother's blood instead of being consumed by the cells. This condition is called hyperinsulinism which refers to a higher than normal level of insulin in a patient's blood. During normal pregnancy, certain metabolic chances occur with the ricks of motherly obesity and hyperglycemia on the woman and the fetus, as well as neonatal outcomes. Can fetus abnormally secrete insulin? Before answer this question we need to answer first the following question. What are the metabolic chances that occur in pregnant women? As the placenta grows or as the pregnancy advances, the following metabolic changes can happen:

a) Insulin resistance (IR) and the amount of insulin produced upsurges, in response to the increase of glucose concentration. In this case increased IR is linked with unsuccessful maternal and fetal outcomes [1].
b) More placental hormones are produced, and the risk of insulin resistance becomes greater. Normally, the pancreas is able to make additional insulin to overcome insulin resistance, but when the production of insulin is not enough to overcome the effect of the placental hormones, gestational diabetes results [2,3].
c) High glucose concentrations are known to promote B-cell replication [4].
d) So pancreas of the fetus senses the high glucose levels and produces more insulin in an effort to use this excess of glucose [1].
e) Placenta supplies a growing fetus with nutrients and water.
f) Fetus converts the extra glucose to fat [1].

It takes a good development of the fetus and pregnancy in general to avert alterations in the fetal metabolism caused by an abnormal intrauterine environment, whose significances are fatal [4]. It is known that pregnancy induces a stress on the endocrine pancreas and the total organism; this may explain why alterations are also observed in this period. But does abnormal insulin secretion transmits gestational diabetes? Or what causes gestational diabetes? Insulin is the hormone that is secreted by the pancreas and results in the lowering of sugar levels in the blood circulation. In pregnancy, the hormones that are secreted by the placenta make the mother's body less receptive to insulin. This is known as insulin resistance. So during pregnancy, women with GDM are insulin resistant and have imperfect insulin excretion in response to hyperglycemia. This recommended that GDM resulted from a failure of β cells to reward for the upsurge in insulin resistance that happened during late gestation. After childbirth, insulin resistance and insulin emission enhanced, and insulin emission was no longer meaningfully different in women with GDM. This suggests that the decrease in insulin resistance that happened after postpartum reduced the demand for insulin emission and allowed β cells to function more typically despite a persistent β cell deficiency [5]. The typical B-cell hyperplasia (increase in the reproduction rate of cells) in fetuses of diabetic mothers only happens if the fetus has an operational hypothalamo-hypophyseal system, stressing the contribution of other hormonal regulatory mechanisms. Additionally, fetal hyperglycemia induces fetal hyperinsulinemia, known to alter the ventromedial portion of the hypothalamus, which controls insulin secretion by controlling vagus nerve tone [4]. It is also important to mention that normalization of the diabetic intrauterine milieu in the last part of pregnancy protects B-cell function and the hypothalamus [6].

Fetal hyperinsulinemia, follow-on from hypoplasia (underdevelopment or imperfect enlargement of a tissue or organ) of the endocrine pancreas in maternal and fetal undernourishment or follow-on from B-cell exhaustion in severe diabetes, might have a contradictory effect. Fetal hypoinsulinemia presents a lack of stimulation for the enlargement of the insulin receptor system and this may affect insulin-sensitive organs in an assorted manner. The influence on the fetal endocrine pancreas and other fetal systems be determined by the metabolic disorder of the mother including motherly diabetes connected with hyperglycemia and motherly undernourishment or reduced utero-placental circulation associated with hypoglycemia most probably have assorted properties on fetal metabolic processes or gene expression [6].

Hypoinsulinism is unconditional or relative insulin insufficiency which produces a disease called diabetes mellitus. Hyperinsulinism is the excessive production of insulin by tumors of the pancreatic β cells. Patients suffering from this condition undergo hypoglycemic crises, weakness, intense sweating, and dizziness. If the modification is not treated by providing glucose, patients can suffer a hypoglycemic shock, with loss of intellectual capacity, seizures, coma, and even death. Women with GDM had a major β-cell deficiency that made it impossible for them to compensate for their enlarged level of insulin resistance, which occurred during late pregnancy [7,8]. Several types of major birth anomaly including a birth anomaly of the lower spine, a birth anomaly of the brain, and limb anomalies, are risks significantly provoked by pre-existing diabetes [9].

Role of Insulin Therapy

Insulin therapy is beneficial in restoring glycaemia in women with GDM. Insulin therapy permits in newborn normoglycaemia and reduces macrosomia (a newborn who's much larger than average) incidence in GDM. Insulin therapy and diet approaches are apparently equally effective in normalizing the maternal glycaemia. The placenta, fetus, and newborn are positively and negatively impacted by insulin therapy [10]. Nevertheless, despite these rapid developments in insulin therapy, there are still many open questions that include: what could be the role of factors other than gestational hormones in the development of insulin resistance during pregnancy? What could be the post-binding anomalies leading to an abnormal function of the insulin receptor during gestation? What about insulin and fetal growth? Is the fetus less insulin resistant than its mother? Are children born to mothers with gestational diabetes heavier and more labile in blood sugar due to higher insulin sensitivity? [11].

These difficult questions to answer stimulate another question allowing orienting the research towards a tentative of solutions in African medicine. Do antidiabetic already known plants help to control the hyperinsulism in pregnant diabetic women? Or Can antidiabetic plants more economical and available, taken by indigenous gestational diabetics control GDM?

Methodology

To identify previous work used to write this article a systematical search was done using four engines:

a) "Abnormal insulin secretion in GDM" as engine which permits us to identify two abnormal insulin secretions in gestational diabetes: hypoinsulism and hyperinsulism;
b) "Antidiabetic plants help to control the hyperinsulism in pregnant diabetic women or animals" Plants that caught our attention are plants already used by hinterlands diabetic women in Cameroon;
c) "What organs secrete insulin during pregnancy". This engine enables us to identify fetus 'organs and mother's organs;
d) "Toxicity of a given recorded plant name" used to verify the harmlessness of recorded plants. Recent relevant articles, published in English language between 1970 and 2020 were selected for global appraisal.

Results

Pharmacologically screened insulin mimetic, insulin sensitivity or insulin release by identified plants, used in Cameroon and their phytoconstituents.

Antidiabetic Plants with Diabetic Effects Demonstrated in Clinical Trial

Momordica charantia L. (Curcubitaceae)

The treatment of patients suffering from hyperinsulinemia with a nutraceutical primarily constituted of the extract of *Momordica charantia* and the antioxidant alpha lipoic acid may be considered as a substituted for the conventional pharmacological method. In this opening trial, including a limited number of cases, the nutraceutical was found to be operative as for as biological indicators were concerned. It was well stomached and without toxicity [12]. Antidiabetic plants increased insulin sensitivity or insulin secretion or any hypoglycemic properties in gestational diabetic-induced animals.

M. charantia (Bitter melon) supplementation has been reported to improve the insulin sensitivity in hyperinsulinemia. It enhanced insulin resistance and reduced serum insulin and leptin in rats fed with a high fat diet. In skeletal muscle it increases insulin sensitivity by enhancing skeletal muscle insulin-stimulated IRS-1 tyrosine phosphorylation in high-fat-fed rats. A current research confirmed that polypeptide found from the plant binds with IRs and controls downstream insulin signalling pathway [11]. *Momordica charantia* contains numerous biologically active chemical compounds such as glycosides, saponins, alkaloids, fixed oils, triterpenes, proteins, and steroids. *M. charantia* contains a number of chemical compounds including important vitamins, minerals, antioxidants, and numerous other phytochemicals including glycosides, saponins, phenolic constituents, fixed oils, alkaloids, reducing sugars, resins, and free acids. The immature fruits are also good source of vitamin C and also provide vitamin A, phosphorus, and iron. Depending on the characteristics nature of the isolated compounds, they can be divided into several groups such as phenolic and flavonoid compounds, cucurbitane type triterpenoids, cucurbitane type triterpene glycoside, oleanane type triterpene saponins, and insulin like peptide [12]. Besides these properties, other scientists have also discovered an insulin secretagogue activity of the plant. Subcutaneous administration of the protein extract isolated from the fruit pulp of *Momordica charantia* augmented plasma insulin levels by 2 times after 4 h of administration. Protein extract from fruit pulp also augmented insulin secretion, but not glucagon in the perfused rat pancreas [13]. A recent research also supporters that saponin significantly encouraged insulin secretion in vitro from pancreatic β cells [14].

Ethno pharmacological preparation: In Cameroon 300g of fresh aerial parts of *Momordica charantia* are boiled in 4 liters of water for 15mn. Drink 2 to 3 glasses daily for a week.

Antidiabetic Plants with Diabetic Effects Demonstrated in Animal Models

Brassica oleracea L. (Brassicaceae)

The administration of *Brassica oleracea* improves the impairment of glucose and lipid homeostasis in HFD-induced obese mice by inhibition of hyperglycemia, hyperlipidemia, hyperinsulinemia and hyperleptinemia. Improvement of glucose and lipid homeostasis by *Brassica oleracea* extract is associated with the reduction of lipogenic gene expressions (SREBP1c, FAS and ACC). Besides, we did not found any health complications or side properties like diarrhea in mice after long-term oral administration of Brassica oleracea. Consequently, the administration of *Brassica oleracea* extract may be a new therapeutic agent for restoring reduced glucose-lipid homeostasis in HFD-induced obesity disorder [15].

Ethno pharmacological preparation: In Cameroon 400g of fresh leaves of *Brassica oleracea* are boiled in 4 liters of water for 15mn. Drink 3 glasses daily for a week.

Zea mays L. (Poaceae) Purple Corn

The HF diet induced hyperglycemia, hyperinsulinemia, and hyperleptinemia, in mice, whereas the same biological environments were not detected in HF mice receiving the purple corn complement. Nevertheless, it is the presence of anthocyanins and other phenolic compounds that sets purple corn apart from other conventional corn varieties and makes it a healthy food. Presently, more than 20 bioactive phenolic compounds, as well as phenolic acids, anthocyanins, and other flavonoids, have been reported to be isolated in purple corn. These phenolic ingredients have been reported in various in vivo and in vitro studies to have powerful health-benefitting abilities including antioxidant, anti-inflammatory, anti-mutagenic, anti-carcinogenic, anti-cancer, anti-angiogenesis properties. They can help to improve lifestyle sicknesses like obesity, diabetes, hyperglycemia, hypertension, and cardiovascular diseases [15].

Ethno pharmacological preparation: In Cameroon 300g of purple corn powder are boiled in 4 liters of water for 15mn. Filter and drink 3 glasses daily for a week.

Scoparia dulcis L. (Scrophulariaceae)

Scoparia dulcis has the potential to be regarded as a hypoglycemic medicinal plant based on its good glucose transport properties and its insulin secretagogue activity [16].

Ethno pharmacological preparation: In Cameroon 300g of *Scoparia dulcis* aerial parts are boiled in 4 liters of water for 15mn. Filter and drink 3 glasses daily for a week.

Cucurmis longa L. (Zingiberaceae)

In vivo animal researches examining the effects of curcumin show noteworthy improved glucose and lipid homeostasis. Serum glucose and lipid levels were significantly reduced. Oxidative stress and lipid peroxidation were reduced with curcumin treatment, while antioxidant enzyme activities were increased. In addition, pro-inflammatory cytokine levels and macrophage infiltration to adipose and liver tissues were reduced. Furthermore, mitochondrial biogenesis was improved with curcumin administration. Administration of curcumin to animal models of diabetic nephropathy resulted in improved kidney function [17].

Ethno pharmacological preparation: In Cameroon 300g of *Cucurmis longa* powder are boiled in 3 liters of water for 10mn. Filter and drink 3 glasses daily for a week.

Acacia arabica L. (Fabaceae-Mimosoideae)

About 94% of *Acacia arabica* seed diet exhibited hypoglycemic activity in rats through production of insulin. However, *Acacia arabica* seeds powdered at 2, 3 and 4 g/kg, p.o. exerted a noteworthy hypoglycemic effect in normal rabbits by releasing insulin from the beta-cells of Langerhans [18,19].

Ethno pharmacological preparation: In Cameroon 300g of *Acacia arabica* seeds powder are boiled in 3 liters of water for 10mn. Filter and drink 3 glasses daily for a week.

Aloe barbadensis Gheequar (Aloeaceae)

The extract of *Aloe barbadensis* leaves stimulated the synthesis and the release of insulin in and significantly decrease the glucose level in streptozotocin induced diabetic rats [18,19].

Ethno pharmacological preparation: In Cameroon 400g of *Aloe barbadensis* leaves are macerated in 2 liters of water for 40mn. Filter and drink 3 glasses daily for a week.

Aloe vera (L.) Burm.f. (Aloeaceae)

Hypoglycemic effect by Aloe vera gel in the rats is facilitated by the synthesis or release of insulin from pancreatic beta cells. Effect of pseudoprototinosaponin AIII and prototinosaponins AIII on glucose uptake and insulin secretion suggested their hypoglycaemic activities are due to actions on liver gluconeogenesis or glycogenolysis. Repeated doses *Aloe vera* bitter principle revealed hypoglycemic

activities in diabetic rats, which was through stimulus of synthesis or secretion of insulin from pancreatic beta cell [18,19].

Ethno pharmacological preparation: In Cameroon 400g of Aloe vera leaves are macerated in 2 liters of water for 40mn. Filter and drink 3 glasses daily for a week.

Annona squamosa (Annonaceae)

Annona squamosa possesses antidiabetic effect that acts by promoting insulin secretion from the pancreatic islets, increasing glucose uptake in muscle and inhibiting hepatic glycogenesis [18].

Ethno pharmacological preparation: In Cameroon 400g of *Annona squamosa* stem bark are boiled in 3 liters of water for 12 mn. Filter and drink 3 glasses daily for a week.

Boerhaavia Diffusa Punamava (Nyctaginaceae)

Hypoglycemic and antihyperglycemic effect of aqueous leaf extract at 200 mg/kg p.o. for 4 weeks in normal and alloxan induced diabetic rats revealed to upsurge plasma insulin levels and increase glucose tolerance [19].

Ethno pharmacological preparation: In Cameroon 400g of *Boerhaavia diffusa* roots are boiled in 3 liters of water for 10mm. Filter and drink 3 glasses daily for a week.

Zingiber officinale Adrak Zingiberaceae

Treatment with *Z. officinale* increase insulin level, decreases fasting glucose level, decreases serum cholesterol, serum triglyceride and blood pressure in diabetic rats. Our data suggest a potential antidiabetic activity of the juice of *Z. officinale* in type I diabetic rats [20].

Ethno pharmacological preparation: In Cameroon 400g of *Zingiber officinale* rhizomes are boiled in 3 liters of water for 10mm. Filter and drink 3 glasses daily for a week.

Ipomoea batatas (L.) Lam. (Convolvulaceae)

The antidiabetic potential of *Ipomoea batatas* extract is due to the presence of bioactive constituents that include glycoprotein, anthocyanins, alkaloids, and flavonoids, which act as insulin mimetic molecules or insulin discharge constituents in sweet potatoes peel-off. *Ipomoea batatas* also reduces insulin resistance and blood glucose level [21].

Ethno pharmacological preparation: In Cameroon 400g of *Ipomoea batatas* tuber are boiled in 3 liters of water for 10mm. Filter and drink 3 glasses daily for a week.

Discussion

It exist two types of hyperinsulinism treatment:

- Treatment of Congenital Hyperinsulinism (CHI) or Persistent Hyperinsulinemic Hypoglycemia of Infancy (PHHI): Instantaneous treatment of hypoglycemia is indispensable to an intensive care unit (ICU) or a neonatal ICU (NICU) until blood glucose level becomes stable. Patient newborn may require uninterrupted intravenous (IV) glucose infusion. Glucagon may also be administered emergently to maintain adequate blood glucose levels. The primary medications used in long-term treatment of CHI include diazoxide, octreotide, and nifedipine [22].
- Treatment of Neonatal Hyperinsulinism: For infants with such symptoms lethargy, coma, or seizures from hypoglycemia we endorse administering parenteral glucose (Grade 1C). Therapy should be started while awaiting laboratory confirmation. We begin with an intravenous (IV) bolus of dextrose (200 mg/kg) over 5 to 15 minutes (2 mL/kg of 10 percent dextrose in water). This is followed by the uninterrupted administration of parenteral glucose infusion at an initial amount of 5 to 8 mg/kg per minute. If hypoglycemia is insistent, glucose infusion rates should be improved as needed [23].

These curative treatments are not easy to accomplish, especially in developing countries. It is necessary to privilege the natural preventive treatments namely physical exercises and treatment by plants. The analysis of recorded plants shows that using of medicinal plants with antidiabetic extracts and compounds improve very well the following activities:

- insulin secretion,
- insulin sensitivity in hyperinsulinemia,
- glucose uptake,
- decreasing fasting glucose level,
- decreasing serum cholesterol,
- decreasing serum triglyceride
- increasing glucose tolerance,
- reduction of blood pressure
- or which act as insulin mimetic,
- act as insulin discharge constituents,
- inhibiting hepatic glycogenesis,
- show noteworthy improved glucose and lipid homeostasis,
- enhance insulin resistance and reduced serum insulin and leptin,
- Contain numerous antidiabetic active chemical constituents such as glycosides, saponins, alkaloids, fixed oils, triterpenes, proteins, and steroids, flavonoids, phenols, etc.

Many other species of genus Annona, Aloe, Ipomoea, Momordica and Euphorbia were used in self-medication by diabetic pregnant women.

The recorded plants are less toxic at therapeutic doses:

1. ***Momordica charantia L.*** **(Cucurbitaceae):** Haematological evaluations did not show significant differences in white blood cells count, mean corpuscular volume and mean corpuscular haemoglobin concentration levels. The LD50 of the ethanolic extract of *Momordica charantia* is considered safe to be consumed below 2000 mg/kg. However, the study indicates that the highest dosage could provoke the toxic effects to the blood, tissue and vital organ especially liver [24].
2. ***Annona squamosa*** **(Annonaceae):** Acute toxicity study carried out on ingestion of 800mg/kg, 1600mg/kg and 5000 mg/kg body weight showed no toxicity observed at 800mg/kg and 1600mg/kg doses. At 5000mg/kg body weight dose 100% death was recorded within 24 hours [25].
3. ***Aloe barbadensis Gheequar (*****Aloeaceae*****):*** Toxicity in the genus Aloe should be controlled. This is why in ingredients derived from Aloe vera used in cosmetics regardless of the species, anthraquinone levels should not exceed 50 ppm. For the expert group on the review of cosmetic ingredients, industry should ensure that the total polychlorinated biphenyls/pesticides contamination of any cosmetic ingredient of plant origin should not exceed 40 ppm, with no more than 10 ppm for any specific residue. They must be appropriate for the following impurities: arsenic (3 mg / kg maximum), heavy metals (20 mg / kg maximum) and lead (5 mg / kg maximum) [26].
4. ***Cucurmis longa*** **L. (Zingiberaceae):** From *Cucurmis longa* 200 constituents were identified, 184 constituents were expected as toxigenic, 136 constituents are mutagenic, 153 constituents are carcinogenic and 64 constituents are hepatotoxic [27].
5. ***Acacia nilotica*** **L. (Fabaceae-Mimosoideae) Synonymes:** *Acacia arabica* (Lam.) Willd. (1806), *Acacia scorpioides* (L.) W. Wight (1905). *Acacia nilotica* aqueous bark extract revealed to be safe in single dose given to mice. But it was observed that repeated administrated doses higher than 250 mg/kg body weight of the extract for 28 days in rats may provoke hepatotoxicity [28].
6. ***Boerhaavia diffusa Punamava*** **(Nyctaginaceae):** In animal models there were no noteworthy changes in both the absolute and relative organ weights between the witnesses and tested groups. The hepatic enzymes and haematological parameters were statistically identical in all the groups [29].
7. ***Ipomoea batatas*** **(L.) Lam. (Convolvulaceae):** The toxicity in *Ipomoea batatas* presents the following illnesses: pulmonary oedema, emphysema and adenomatosis in cattle. These disease signs have also been recognized to other prepared feed products, silage and lush pasture grass. Slightly similar properties have been detected when large doses of tryptophan were administered to cattle [30].
8. ***Zea mays*** **L. (Poaceae) Purple corn:** *Zea mays* exposed to Cd stress increases significantly Cd concentration in all plant parts predominantly in roots. The cultivar Wan Dan 13 stored moderately higher Cd in roots, stems, and leaves than Run Nong 35. Nonetheless, in seeds, Run Nong 35 recorded higher Cd levels. The grain yield of maize was considerably decreased chiefly for Run Nong 35 under different Cd toxicity levels as compared with control [31].
9. ***Scoparia dulcis*** **L. (Plantaginaceae):** *Scoparia dulcis* extract was established to be non-toxic with LD50of 3807(mg//kgbody weight). The plant extract also revealed a good immunostimulatory effect with a noteworthy increase in white blood cell propagation when administered into mice at doses of 100 and 1000mg/ml. The result of this investigation supports the popular use of this plant for the traditional remedy of pneumonia possibly caused by these test organisms and as blood tonic [32].
10. ***Aloe vera*** **L. (Aloeaceae):** Aloe vera is potentially toxic, with side effects occurring at some dose levels both when ingested and when applied topically. Although toxicity may be less when aloin is removed by processing, Aloe vera ingested in high quantities may induce side effects, such as abdominal pain, diarrhea or hepatitis [33].
11. ***Brassica oleracea*** **L. (Brassicaceae):** In studies there was no mortality or any significant changes noticed in the SD rats after the administration of established plant extract of 300, 2000 and 4000 mg/kg body weight respectively. The experimental animals did not showed any drug related changes in behavior, breathing, skin effects, water consumption, impairment in food intake and temperature. Furthermore *B. oleracea* Var. Italica extract did not produce any remarkable change in biochemical and hematological parameters following the administration of tested crude plant extract of 400 and 8000 mg/kg body weight for 28 consecutive days [34].
12. ***Zingiber officinale*** **L. (Zingiberaceae):** *Zingiber officinale* showed no evidence of toxicity and death in the acute and subacute toxicity testing with the maximum tolerated dose (MTD) of 5000 and 2000 mg/kg body weight, respectively [35].

Toxicity studies are necessary for clinical and traditional applications, for safe consumption and medical use. They are also important for the use of each of the 12 plants as a remedy at a recommended dosage.

Conclusion

At the end of this study 12 plants used in Cameroon for diabetic management can be helpful in the treatment of polyinsulinism more characteristic of GDM and in the

regulation of hypoinsulism in mother with GDM. The principal pathways of action were insulin sensitivity improvement and insulin resistance impairment. With less toxicity, many of these herbs may be opportunities to implement strategies to improve the risk of cardiovascular disease of the mother in addition to that of her offspring and may offer the potential to reduce the intergenerational risk of obesity, diabetes and other metabolic disturbances. *Momordica charantia* L. is the most important less toxic plant possessing over 225 changed medicinal ingredients. These different phyto-constituents may act either distinctly or together to exert their medicinal activities. In addition this plant and as far as diabetes concern, contains charantin, insulin-like peptide and alkaloid-like extracts possess hypoglycemic properties similar to the plant itself or its crude extracts. These different compounds seem to exert their beneficial effects via several mechanisms to control and treat low and high insulin secretion in gestational diabetes mellitus. We remorse the few number of available clinical data as reviewed in the present article dominated by the abundant data from animal studies that are frequently not applicable to human beings. The present article supports the need for better-designed clinical trials with sufficient sample size and statistical power to further indicate the acclaimed efficacy of the 12 plants in the fabrication of phytodrugs more cheap and efficient for gestational diabetes mellitus worldwide. The three species, *Momordica charantia*, *Zingiber officinale* and *Brassica oleracea* may be a feasible option for resilient communities in developing countries and especially for poor pregnant women of hinterlands who have a high prevalence of gestational diabetes and depend only from herbal medicines, according to their cultural and spiritual beliefs. However the study of toxicity on samples of plants collected in Cameroon remains an absolute necessity.

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