

Hunteria Umbellata Extract is a Potent Agent for Effective Diabetes Control

ABSTRACT:

Background: As many as 422 million of the world population, which is 8.5% of the global population were suffering from diabetes in 2014, in 2016, diabetes as a cause of death rose by 5%, and 1.5 million lives were lost to diabetes in 2019 hence, solution-driven interventions to bring the diabetes epidemic under control is necessary. Medications to treat are too expensive for the poor and have adverse side effects that stand in the way of treatment thus, the demand for affordable and harmless herbal alternative is on the rise, and many Africans use *Hunetria umbellata* to treat diabetes. **Objectives:** Conduct a review of clinical epidemiological studies performed to determine *Hunteria umbellata* extract efficacious potency in controlling sugar and diabetes. Purpose is to encourage and promote its proper use if evidence supports its use, or discourage its use if evidence states the contrary. **Methods:** A systematic review study that used various search engines to locate, assess, review, and summarize clinical studies conducted to investigate the potency of *Hunteria umbellata* extract in blood sugar and diabetes control. Samples size was $n=22$ studies reviewed. Search words were "*Hunteria umbellata* , *composition of Hunteria umbellata* , *Hunteria umbellata and diabetes*, *Hunteria umbellata and sugar*". **Results:** Results revealed that *Hunteria umbellata* extract is a potent agent for controlling blood sugar and diabetes significantly, its effect manifests after six hours and its sugar reduction action continues progressively over time as the dose and concentration increases. **Conclusion:** *Hunteria umbellata* extraction in all clinically approved standards of extraction showed straight antagonism to blood sugar and diabetes, it is a potent agent against sugar and diabetes thus, its use in Africa as native medicine for treating diabetes is justified.

Keywords: [Hunteria umbellata, Diabetes, Control, Diabetes control with Hunteria umbellata, African Native medicine]

1. INTRODUCTION

Researchers have revealed that *Hunteria umbellata* is a plant with high medicinal value and potent antagonism to sugar, cholesterol, obesity, and hypertension, and Africans have used *Hunteria umbellata* as a native medicine for treating diabetes Mellitus type II (6, 1, 7, 8, 9, 11, 13, 14). Thus, conducting this kind of study to succinctly assay the evidence conducted locally and internationally about *Hunteria umbellata* is necessary to determine its efficacious remedies for preventing and controlling diabetes Mellitus type II, which is a high ranking (1) global disease pandemic that is causing premature deaths, disabilities, unbearable pains, and huge financial loss to individuals, families, and various governments (2, 3, 4, 5).

The purpose of this study is to determine whether *Hunteria umbellata* is an affordable medicine for treating diseases that are out of reach for the poor and middle class especially, those in developing countries where clinical and hospital visits are only accessible for those who can afford them. In cases where modern medicine could not offer remedies, native medicines can offer hope if efficacious. Additionally, this paper combines a collection of peer-reviewed literature making information on *Hunteria umbellata* easily accessible to busy clinicians who lack the time to go through countless of such studies to find consensus evidence.

This is a systematic review, also called community guide to preventive services that seeks a succinct assay of peer reviewed evidence about *Hunteria umbellata*'s antagonism to sugar and diabetes, thus in this study the question is to determine if *Hunteria umbellata* extract can significantly prevent diabetes and control blood sugar.

Justification/Background/Problem Statement

Diabetes is a global disease pandemic that is affecting hundreds of millions of people worldwide and killing millions of people every year, hence, solution-driven interventions to bring the diabetes epidemic under control is necessary (1). Medications to treat are too expensive for many and have adverse effects that stand in the way of treatment. There is a high and growing demand for affordable and harmless herbal remedies for controlling diabetes and metabolic syndrome diseases worldwide because people feel it is affordable and safe to use (1, 7, 8, 9, 11, 13, 13, 14). Though, Africans use *Hunteria umbellata* to treat diabetes, some are unsure and lack the confidence and self-will to use it, some are using it wrongly, either under dose or overdose. And some think that it is superstitious to use *Hunteria umbellata* to treat diseases especially serious diseases like diabetes.

The World Health Organization stated that 80% of global diseases are treated using medicinal plants in poor countries of the world, and actually, plant medicine is the only accessible health care in poor rural communities (1). Diabetes is a pandemic disease of global concern; it is a metabolic syndrome disease that has characteristics of high blood sugar, and in a prolonged case causes harm to the blood vessels, nerves, heart, kidney and eyes. There are two types of diabetes, Type I and type II. Type I diabetes occurs in childhood, which is also called juvenile diabetes, and depends solely on insulin for treatment because the body can only produce a little insulin. Type I is not common; but the type II diabetes is common (2). Type II diabetes is usually developed at an adult age because the body fails to produce enough insulin or that enough insulin is produced but is too weak and not able to digest and control sugar levels in the blood (2). Today, diabetes has been diagnosed in 422 million people globally, in 2014 and 1.5 million people pass away yearly in 2019 because of diabetes.

In Canada 7.8% of males and 6.5% of females are diabetic, a total of 7.2% of Canadian population suffering from diabetes. There are factors that place Canadians at risk of diabetes namely, overweight, 67.7%, next is obesity, 30.1%, and physical inactivity, 25.9% (3).

Also, WHO indicated that the diabetes prevalence in Nigeria is 4.4% of males and 4.3% of females, and a total of 4.3% of the Nigerian population having diabetes. The risky behavior variables that can cause diabetes are that 30.1% of the Nigerian population is overweight, 9.7% have obesity and 19.8% are physically inactive (4).

Additionally, in 2016, the World Health Organization indicated that diabetes in the United States of American population is a significant health concern with nearly 10% (9.8%) of

males, and 8.3% of females having diabetes, and a total of 9.1% of the USA population having diabetes. The United States population with risky behavior factors that can cause diabetes are, 69.6% of American population having overweight, over one third, 35.0% living with obesity, and excess of one third, 35.0% were physically inactive. As we can see, diabetes remains a disease of global concerns affecting poor and rich countries alike (5). In all these, health promotion directed at addressing these factors are necessary.

While a significant amount of the global population is living with diabetes, a significant amount of the worldwide population cannot afford costly medical treatment of diabetes. Up to 80% or more depend entirely on plant medicine. Also, some who can afford medical treatments are heavily weighed down by adverse effect of some diabetes medications.

These reasons have led to a growing use and demand of herbal remedies because it is cheap and some believe that it is effective for treating diseases. Since African use *Hunteria umbellata* as native medicine for treating diabetes and other diseases (1, 7, 8, 9, 11, 13, 13, 14). A need for evidence is now a crucial necessity to validate or debunk its efficacy for diseases treatment. Evidence testing herbal medicine efficaciousness for diseases control is not as sufficient as the synthetic medicines thus, this kind of study is necessary to fill this gap.

2. METHODS

In this systematic review study, authors reviewed the efficaciousness of *Hunteria umbellata* in controlling blood sugar through an assay of a pool of clinical studies performed in this regard. The purpose was to support and promote proper use of *Hunteria umbellata* for controlling sugar and diabetes if, evidence was adequate, or to discourage the native use of *Hunteria umbellata* to treat sugar and diabetes if evidence suggested the opposite. Also studied was the composition of *Hunteria umbellata* extracts to further make an easy link to its native use for diabetes and sugar control.

Only peer reviewed clinical studies performed using epidemiological standards, which were freely available online were included in the pool of clinical researches from which this study was conducted. The studies were conducted on *Hunteria umbellata* root and stem bark extract, fruit extract, seed extract and leaves extracts. Not all clinical studies reviewed were reported to avoid redundancy, and only the summary of some evidence were presented. Sample size was n=22, and some of these studies reviewed many other studies performed about *Hunteria umbellata*.

Various search engines namely google, google scholar, bing, and Firefox were used to search for required evidence, and the search words were, *Hunteria umbellata*, composition of *Hunteria umbellata*, *Hunteria umbellata* and diabetes, *Hunteria umbellata* and sugar. Studies that did not follow epidemiology standard, were not available freely online, and were not peer reviewed were excluded. Only the summary of the studies are presented here. Next are the results.

3. RESULTS AND DISCUSSION

The results suggest that based upon the composition and clinical evidence, *Hunteria umbellata* is significantly potent in preventing and controlling sugar and diabetes (1, 7, 8, 9, 11, 13, 13, 14). Eight of the reviewed and selected articles are presented next.

Evidence1.

These authors (6) investigated the justification of use of *Hunteria umbellata* water extract as native medicine for treating diabetes, obesity, anemia, stomach ulcers, pain and labor pains and ascertained the possible toxicity and reversibility of the toxicities. The purpose was to provide cautionary clues to ensure the safety of users, through the study of *Hunteria umbellata* oral and intraperitoneal- cavity or intestine injection of the substance toxicity. Results, although serum ALP concentration increased during treatment yet, *Hunteria umbellata* extract effects on serum AST and ALT were not significant, which suggests that *Hunteria umbellata* extract has no adverse effect on liver functions and the positive effect of *Hunteria umbellata* extract on serum electrolytes, creatinine, and urea suggested that there is oral safety of *Hunteria umbellata* water extract on kidney function showing a potential to protect the nephritis-kidney inflammation that causes difficulty with waste removal from the body.

Chronic use showed low concentrations of bicarbonate, which is an indication of potential for metabolic acidosis. Meaning that overuse or chronic use should be avoided. Also, chronic use indicated low level and reversible presence of histological lesions. High concentrations of phytochemicals namely, flavonoids and alkaloids were a reason for the liver and kidney protection because these compounds have significant evidence of preventing tissue per oxidation through free-radical prevention and antioxidant ion function thereby providing protection to kidney and liver tissues.

The results about tissue proliferation raise some question about the accuracy because, the magnifications of pictures of the various organs were not harmonized, some were magnified by 40, some 400 raising some questions about the claim of tissue proliferation, also the inter peritoneal *Hunteria umbellata* administration is not practical with humans but more practical with animals.

Hunteria umbellata water extract is relatively safe for acute and chronic use but, high caution is required for prolonged use to avoid tissue proliferation.

Evidence 2.

This authors (7) used Gas Chromatography Mass Spectrometry (GC-MS) and molecular docking to determine the phytochemical compounds in *Hunteria umbellata*, particularly to examine the peroxisome proliferator-activated receptor gamma (PPAR- γ) antagonists concentrations of the phytochemical compounds because those compounds are known to be effective for treating diabetes and sugar through insulin sensitization and inhibition of sugar production in the liver. The results showed that 21 phytochemical compounds were detected from seed and leave extract including 2,2-Benzylidenebis (3-methylbenzofuran). The 2,2-Benzylidenebis of the seed scored -11.3 kcal/mol for fitness and this compound has strong anti-diabetic property (capability). The 2,2-Benzylidenebis and phytochemical compounds of *Hunteria umbellata* seed extract showed a significant anti diabetic effect on PPAR- γ , and the molecular binding interaction recorded in the in-vitro data confirms specifically that 2,2-Benzylidenebis binds to PPAR- γ suggesting it to be a potent compound for treating diabetes. More In-vitro and in-vivo studies to determine mechanisms of action on type II diabetes was recommended. *Hunteria umbellata* seed extract on the account of its phytochemical compound composition is a potent agent against diabetes.

Evidence 3.

Africans used dry seeds of *Hunteria umbellata* K. Schum as a native medicine for treating different types of diseases namely, obesity, diabetes, hypertension, and other diseases. These researchers (8) examined the science behind using *Hunteria Umbellata* seed extract to treat hyperglycemia and obesity. In this study, rats with normal sugar scientifically called normoglycemic rat, and rats whose high blood sugar was caused by high fructose diet or high alcohol consumption were compared. The rats were given 50 mg/kg, 100 mg/kg and 200 mg/kg doses of *Hunteria umbellata* extract daily for a period of the study.

Also, investigated was the oral toxicity of *Hunteria umbellata* seed extract. Preliminary or pre-test as well as intervention test that employed OECD/OCDE Up and Down Procedures Test Guidelines to determine oral toxicity. The results revealed that the extract was rich in phytochemical compounds namely, Flavonoids, tannins, alkaloids, and glycosides. And there was progressively significant decrease in the blood glucose of the *Hunteria umbellata* extract treated animals based upon dose over time. The higher the dose, the greater the blood sugar level reduction, and *Hunteria umbellata* sugar reduction was significantly higher than that caused by a standard diabetes medicine- glibenclamide. *Hunteria Umbellata* lowered sugar concentrations through inhibition of sugar absorption in the intestine and hepatic synthesis of sugar. At treatment doses no toxicity was observed but at an extremely high dose of LD50 1020 mg/kg were slightly toxic. Based upon the outcome of this study, there is scientific evidence behind the use of *Hunteria Umbellata* seed extract for treating obesity and type II diabetes, *Hunteria Umbellata* extract caused significant reduction in blood sugar concentrations and weight of the experimental animals. Toxicity did not occur with the experimental doses but, only slightly occurred on extremely high dose of 1020 mg.kg thus, justifying the use of *Hunteria Umbellata* as a native medicine for treating type 2 diabetes and obesity (8).

Evidence 4.

These authors (9) took it upon themselves to get to the conclusion of the study about anti diabetes claims on *Hunteria umbellata* seeds extract because they believed that at the time of their study and based upon the information available to them that anti diabetic claims on *Hunteria umbellata* seeds extract were based upon opinion and investigations on this claim were yet to be completed. Thus, the authors thoroughly investigated the scientific evidence behind the claim of *Hunteria umbellata* seeds extract as an anti-diabetic agent, with particular focus upon two compounds scientifically known to be potent inhibitors of alpha-glucosidase namely, N4-chloromethylakuummine and 1beta-D-glucopyranosyl-8-methyl-3-iridene-4, 7-carbolactone. And, yes these two compounds were isolated from *Hunteria umbellata* extract. Thus, a clear indication on a molecular basis of *Hunteria umbellata* seeds extract having the capability to prevent diabetes (anti-diabetes), and that justifies its use as native medicine, and in the authors' own words, *Hunteria umbellata* seeds extract "could serve as templates for new anti-diabetic alpha-glucosidase inhibitors". The claims that *Hunteria umbellata* seeds extract supports diabetes inhibition is no longer an inconclusive or mere opinion, but rather a clear fact that *Hunteria umbellata* seeds extract is a potent anti-diabetic agent.

Hunteria umbellata extract is a potent agent for controlling sugar and diabetes.

Evidence 5.

These authors (10) believe that herbs including *Hunteria umbellata* have been used to treat sexual problems but were unsure if it is true and if yes, how it achieves that. Authors examined *Hunteria umbellata* seeds and *Cylicodiscus gabunensis* (CG) stem bark extracts effect on the main enzymes that cause erection dysfunction namely, arginase, and phosphodiesterase-5 as well as their effect on two main enzymes associated with type II diabetes namely, alpha-amylase, and alpha-glucosidase. Findings stands as, both extracts achieved inhibition of alpha-amylase, (IC₅₀ = 221.30 ug/ml, and alpha-glucosidase (IC₅₀ = 184.35) based upon dose, the higher the dose the greater the inhibition and were greater than phosphodiesterase-5 (CG), IC₅₀ = 611.35 ug/ml, and two extracts inhibited arginase and phosphodiesterase-5 based on dose in vitro. However, *Hunteria umbellata* inhibition was stronger with phosphodiesterase-5 (CG), IC₅₀ = 539.72 ug/ml and arginase 41.53 ug/ml, and *Cylicodiscus gabunensis* showing phosphodiesterase-5 (CG), IC₅₀ = 611.35 ug/m and arginase 47.95 ug/ml. Both extracts were composed of anti-oxidation properties manifested by metal- Fe²⁺ chelating capability and DPPH and alcohol-free radical scavenging properties. Extracts were composed of high levels of phenols namely, Quercetin, chlorogenic acid, gallic acid, ellagic acid and caffein acid examined using HPLC. Both extracts inhibited the main enzymes that cause erectile dysfunction, and diabetes type II. *Hunteria umbellata* extracts are safe and harmless natural and affordable agents for treating erecto genesis disorders, and diabetes (10).

Evidence 6.

In this study, these authors (11) wanted to determine if the *Hunteria umbellata* seeds extract can be formulated into standard medicine pill since it possess potency for healing many diseases. The researchers extracted *Hunteria umbellata* seeds powder, and alkaloids isolated from *Hunteria umbellata* seeds that were then used to evaluate *Hunteria umbellata* hardness, friability, dissolution and disintegration profiles in line with unofficial and standard pill evaluation requirements. The result showed that *Hunteria umbellata* water and purified extracts were able to be formulated into tablets and the formulation. Standard tablets formulated from aqueous and purified extracts obtained from *Hunteria umbellata* seed powder met standard requirement for tablets formulations of dissolving or disintegrating in less than 15 minutes. *Hunteria umbellata* has potency against diseases and it is used traditionally in Southern Nigeria to treat multiple diseases. (11) A similar study that investigated *Hunteria umbellata* suitability for pill formulation, the authors suggested that *Hunteria umbellata* extract can be formulated into Microencapsulation (12).

Evidence 7

In this research, authors (13) conducted an evaluation of *Hunteria umbellata* anti hyperglycemic effect on experimental animals as well as the mechanism of function of water extract of *Hunteria umbellata* seeds on alloxan-induced hyperglycemic rats and normal rat used for this clinical experiment. It was a *Hunteria umbellata* chloroform partition test involving, acetyl acetate and butan-1-ol, which formed chloroform fraction, butanol fraction,

ethyl acetate fraction and the residue. In 5% Tween 20 distilled water, 200 mg/kg of each fraction was dissolved. An investigation was performed to determine *Hunteria umbellata* acute oral hypoglycemic effect on the experimental rats for six hours plus. Doses were repeated, and after each treatment dose, an evaluation was conducted, treatments were repeated for five days plus to determine its effect on normal rat and alloxan-induced hyperglycemic rats. In the second analysis, 50 mg/kg crude extract of *Hunteria umbellata* alkaloid fraction was analyzed for anti hyperglycemic function in alloxan-induced hyperglycemic rats with oral glucose tolerance test after six hours of dose administration. The Dragendorffs reagent chromatography stain of the extract to determine presence of alkaloids qualitatively was also performed. The results of the first experiment revealed significant hypoglycemic action when 200 mg/kg of *Hunteria umbellata* seed extract for the chloroform fraction, acetyl acetate fraction, butanol fraction and the residue, which were dose and time dependent. Butan-1-ol extract fraction caused the highest reduction of sugar. Oral treatment and five days repeat of the treatment resulted in significant reduction in fasting blood glucose levels in the alloxan-induced hyperglycemic rats administered with 200 mg/kg of *Hunteria umbellata* seed extract and butanol extract again resulted in the highest reduction. Additionally, 50 mg/kg oral pre-treatment showed a significant rise in post glucose absorption levels from day 1-day 6 in the same experimental rats for oral glucose tolerance test. There was a high concentration of alkaloids in *Hunteria umbellata* seed extract, which was responsible for its anti-hyperglycemic function as well as its prevention of glucose uptake in the intestine (13).

Evidence 8

In this study, the authors (14) conducted a systematic review of *Hunteria umbellata* extract native use for controlling obesity and diabetes in West Africa, Nigeria. The focus of this investigation was to determine *Hunteria umbellata* extract's effect on insulin resistance, inflammation, dyslipidemia, and oxidative stress caused by consumption of high fructose diet by the experimental rats studied for nine weeks. The seven groups ranging from A-G were examined. Two control groups A and C were given control diets, and groups B, and D-G were fed high fructose diet for nine weeks. The control group C was given, 400, 100, 200 mg/kg body weight of *Hunteria umbellata* daily for 3 weeks beginning from week six to week nine. The results showed a significant reduction in body weight, insulin level, leptin concentration, abdominal circumference, blood sugar, adiponectin and insulin resistance unlike high fructose fed rats that did not received *Hunteria umbellata* extract treatment, showed significant increases in the parameters reduced by *Hunteria umbellata* extract. High fructose fed rats showed significant rise in concentrations of cholesterol, triglycerides, low density cholesterol (lipoprotein), as well as high atherogenic, coronary artery and cardiac indexes, and reduction of high-density lipoprotein (cholesterol). Also, pro-inflammatory factors namely, tumor necrosis factor-alpha, interleukin-6 and interleukin-8 increased among the high fructose fed rats. Furthermore, high fructose fed rats showed significant reduction in the enzyme beneficial functions namely, superoxide dismutase, glutathione reductase, glucose 6-phosphate dehydrogenase, glutathione, glutathione peroxidase, and catalase. However, among the *Hunteria umbellata* treated rats all the parameters that increased with high fructose fed rats went significantly lower among rats administered with *Hunteria umbellata* extract. Administration of *Hunteria umbellata* extract significantly altered harmful changes in the experimental rats caused by high fructose diet. *Hunteria umbellata* extract has hypolipidemic, hypoglycemic, and antioxidant properties by prevention of dyslipidemia, inflammation, insulin resistance, and oxidative stress caused by experimental rat metabolic syndrome conditions caused by high fructose diet (14).

Having succinctly presented the summary of eight clinical studies among others that significantly supported the justification of the use of *Hunteria umbellata* extract as native medicine for controlling diabetes next, is a discussion of the results.

4. CONCLUSION

It is clear that the evidence presented in this study speaks for itself that *Hunteria umbellata* extract is antagonistic to sugar and diabetes and it is a significant potent agent in controlling blood sugar and diabetes. Evidence have strongly supported that *Hunteria umbellata* extract, however it was extracted, exerted strong antagonism to sugar and diabetes, and it has

showed a significant reduction of sugar concentration in the blood. Evidence presented in this study was achieved through various means of sugar and diabetes controlled clinical experiments and all results suggested that *Hunteria umbellata* extract reduces sugar and diabetes. So, here is nature responding to the global communities quest for a potent, safe, harmless, and affordable medicine for controlling diabetes that is affecting 422 million of the world population, 2014 and claiming 1.5 million of precious human lives annually, in 2019 (2). *Hunteria umbellata* extract native use as diabetes medicine is justified. *Hunteria umbellata* extract is efficacious in controlling blood sugar and diabetes, and other diseases (1, 6, 7, 8, 9, 11, 13, 13, 14).

It is up the decision makers locally and internationally to see that the *Hunteria umbellata* trees are well taken care of and more *Hunteria umbellata* trees grown to meet the local and global demands for its healing properties for diabetes and other diseases control. Let us initiate action today and not tomorrow to save precious human lives.

CONSENT

N/A

ETHICAL APPROVAL

All authors hereby declares that the approval of Institutional Review Board was not required for this study. This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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