IJBPAS, June, 2017, 6(6): 1304-1314

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

ANTI-DIABETIC EFFECTS OF *BUCHHOLZIA CORIACEA* ETHANOL SEED EXTRACT AND VILDAGLIPTIN ON ALLOXAN-INDUCED DIABETIC ALBINO RATS

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Received 25th Feb. 2017; Revised 25th March 2017; Accepted 20th April 2017; Available online 1st June 2017

ABSTRACT

This study was aimed at evaluating the anti-diabetic effects of *Buchholzia coriacea* ethanol seed-extract and vildagliptin on alloxan-induced diabetic albino rats. Sixty (60) albino rats were grouped into 6 (A, B, C, D, E and F), each group containing 10 albino rats. Diabetes was induced in rats in Groups A, B, C, D and E using 100 mg/kg alloxan via intra-peritoneal administration. Group F was given water and fed without restriction. Rats in groups A, B and C received *B. coriacea* ethanol seed extract at the doses of 100, 200 and 400 mg/kg respectively, while group D received 1.43 mg/kg of vildagliptin daily for 14 days. The rats in group E were not treated and served as negative control. The plasma glucose levels and weights were monitored on daily basis throughout the study period. The results showed dose-dependent reduction in plasma glucose by *B. coriacea* ethanol seed extract. There was a significant ($p < 0.05$) reduction in plasma glucose levels (< 200 mg/dl) in diabetic rats administered 400 mg/kg *B. coriacea* ethanol seed extract (452.75 ± 10.30 to 167.25 ± 6.59) and vildagliptin 1.43 mg/kg (472.00 ± 8.18 to 82.75 ± 6.83) respectively. The body weights decreased dose-dependently and significantly ($p<0.05$) in *B. coriacea* extract groups and there was no significant ($p<0.05$) change in body weight in vildagliptin group. Both *B. Coriacea* ethanol seed extract at higher doses and vildagliptin effectively reduced plasma glucose levels in alloxan-induced diabetic rats.

Keywords: Anti-diabetes, Alloxan, Intraperitoneal, Vildagliptin

INTRODUCTION

Plants are the basic sources of medicines, food, shelters and other items for humans' daily survival (Hemingway, 2004). Medicinal plants have been identified and used throughout human history. Plants have the ability to synthesize a wide variety of chemical compounds that are used to perform important biological functions, and to defend against attack from predators such as insects, fungi and herbivorous mammals. The use of plants as medicines predates written human history. Ethno-botany is recognized as an effective way to discover future medicines. The use of herbs to treat diseases is almost universal among developing countries (Edgar *et al.*, 2002) and is often more affordable than purchasing expensive modern pharmaceuticals. The World Health Organization (WHO) estimates that 80 percent of the population of some Asian and African countries presently uses herbal medicine for some aspect of primary health care. Studies in the United States and Europe have shown that their use is less common in clinical settings, but has become increasingly more common in recent years as scientific evidence about the effectiveness of herbal medicine has become more widely available. The annual global export value of pharmaceutical plants in 2011 accounted for over US$2.2 billion. The use of medicinal plants has evolved over the years in clinical practice. Many herbs have shown positive results *in vitro*, animal model or small-scale clinical tests (Srinivasan, 2005) while studies on some herbal treatments have found negative results (Pittler *et al*., 2000).

Buchholzia coriacea belongs to the family, Capparaceae and is widely distributed in several tropical countries. *B. coriacea* is commonly known as *wonderful kola* . It derived its name from R.W Buchholz who worked on it in Cameroon in late 19th century (Keay, 1989). The leaves and seeds habe been reported to have good antihelmintic (Ajaiyeoba *et al*., 2001), antibacterial (Mbata *et al*., 2009), antimicrobial (Ezekiel and Onyeoziri, 2009), hypoglycemic (Adisa *et al*., 2011), antimalarial (Okoli *et al*., 2010), abortifacient and cytotoxic effects (Adjanohoun *et al*., 1996).

Vildagliptin is an oral anti-hyperglycemic agent of the new dipeptidyl peptidase -4 (DPP-4) inhibitor class of drugs. It inhibits the inactivation of glucagon-like peptide-1(GLP -1) (Ahren *et al.,*2004 and Mentlein *et*

*al.,*1993) and glucose-dependent insulinotropic polypeptide.(GIP) (Mentlein *et al.,*1993) by DPP-4, allowing GLP-1 and GIP to potentiate the secretion of insulin in the beta cells and suppress glucagon release by the alpha cells of the islets of Langerhans in the pancreas. Vildagliptin has been shown to reduce hyperglycemia in type 2 diabetes mellitus (Ahren *et al.,*2004).Vildagliptin is a unique molecule with dual nature as it manages the glucagon levels in hypoglycemia as well as hyperglycemia.

Diabetes is a common non-communicable disease with a sharp rising prevalence in our society. The number of people suffering from diabetes worldwide in 2007 was approximately 246 million (IDF, 2006). It is projected that by 2025 this number will rise to >380 million (IDF, 2006), with most of the increase occurring in developing countries (King *et al*., 1998), where Nigeria belongs. There are several types of diabetes: type I diabetes, type 2 diabetes, gestational diabetes etc. Type 2 diabetes mellitus (T2DM) represents approximately 90–95% of cases of diabetes. T2DM involves two primary pathogenic processes: progressive decline in pancreatic islet function (reduced insulin secretion and inadequately suppressed glucagon secretion) (Weyer *et al.,*1999 and Müller *et al*.,1970) and diminished tissue responses to insulin (insulin resistance) (Weyer *et al.,*1999 and Ahrén and Pacini, 2005). T2DM is managed with synthetic oral hypoglycemic agents and/or insulin (Dhanabal *et al.,* 2007). Type 1 diabetes is a form of diabetes mellitus that results from the autoimmune destruction of the insulin-producing beta cells in the pancreas. The subsequent lack of insulin leads to increased blood and urine glucose. A number of explanatory theories have been put forward, and the cause may be one or more of the following: genetic susceptibility, a diabetogenic trigger, and/or exposure to an antigen (Knip *et al.,* 2005). Type 1 diabetes is mainly treated with exogenous insulin. Gestational diabetes mellitus (GDM) is referred to as any degree of glucose intolerance with onset or first recognition during pregnancy. It develops usually from the 24th week of gestation (Metzger and Coustan, 1998).

Weight management has formed part of the management approaches in the management of several cardiovascular diseases including diabetes. Even though unexplained weight loss may also be seen in uncontrolled diabetes, weight loss in controlled diabetes is associated with improvements in glycaemic

control and cardiovascular disease risk factors. Agents promoting weight loss have beneficial effects on glycaemic parameters, glycaemic control and progression to diabetes (Lloret-Linares *et al.,* 2008). This therefore positions hypoglycaemic agents that also have weight reducing effect as as good alternatives in the management of diabetes. This is because such drugs will improve overall glycemic control (Lloret-Linares *et al.,* 2008).

Even though different types of oral hypoglycemic agents are available along with insulin for the treatment of diabetes, there is an increasing demand by patients to use herbal drugs even when their biologically active compounds are unknown, because of their effectiveness, fewer side effects and relative low cost (Ezeigbo, 2010). These have been the rationale behind the search for very effective, yet affordable and safe alternatives for the management of diabetes.

The prevalence of diabetes demands for more researches focused at alternative and cheaper ways to manage it and ultimately improve patients' quality of life; hence the need to investigate the effect of the ethanol seed-extract of *Buchholzia coriacea* on alloxan - induced diabetic albino rats.

MATERIALS AND METHODS

Materials

The fresh fruits of *B. coriacea* were collected from Ndibe, Afikpo North LGA during the month of August while the adult albino rats were gotten from Abakaliki, both in Ebonyi State, Nigeria. Adult albino rats were obtained from Abakaliki, Ebonyi State.

Chemicals/Reagents

The chemicals and reagents used were of analytical standard.

Methods

Extraction of the Plant Materials

The powdered plant material (800 g) was macerated in 1600ml of ethanol for 48 hours. The mixture was filtered with muslin cloth. The filtrate was concentrated by evaporation to dryness using a rotary evaporator.

Animal Grouping and Induction of Diabetes

The animals were grouped into 6 (A, B, C, D, E and F), each group containing 10 albino rats. The animals in groups A, B, C, D and E were injected alloxan at 100mg/kg body weight via intra-peritoneal route. Those in group F (Control) were given water and fed without restriction.

Administration of *Buchholzia coriacea* Ethanol Seed-Extract and Vildagliptin

Animals in groups A, B, and C were administered the extract at the doses of 100,

200 and 400mg/kg body weight respectively while group D received 1.43mg/kg body weight of vildagliptin and group E received 0.1ml of normal saline. The treatment was administered by oral intubation twice daily for 14 days.

Collection of Blood Samples and Determination of Glucose Levels

The blood samples were collected by vein puncture technique. The plasma glucose levels were measured using a glucometer

Measurement of Body Weights

The body weights were measured on daily basis using electronic weighing balance.

Statistical Analysis

Data was expressed as mean ± Standard Deviation and subjected to one way analysis of variance (ANOVA) followed by Post-hoc LSD using SPSS.

RESULTS

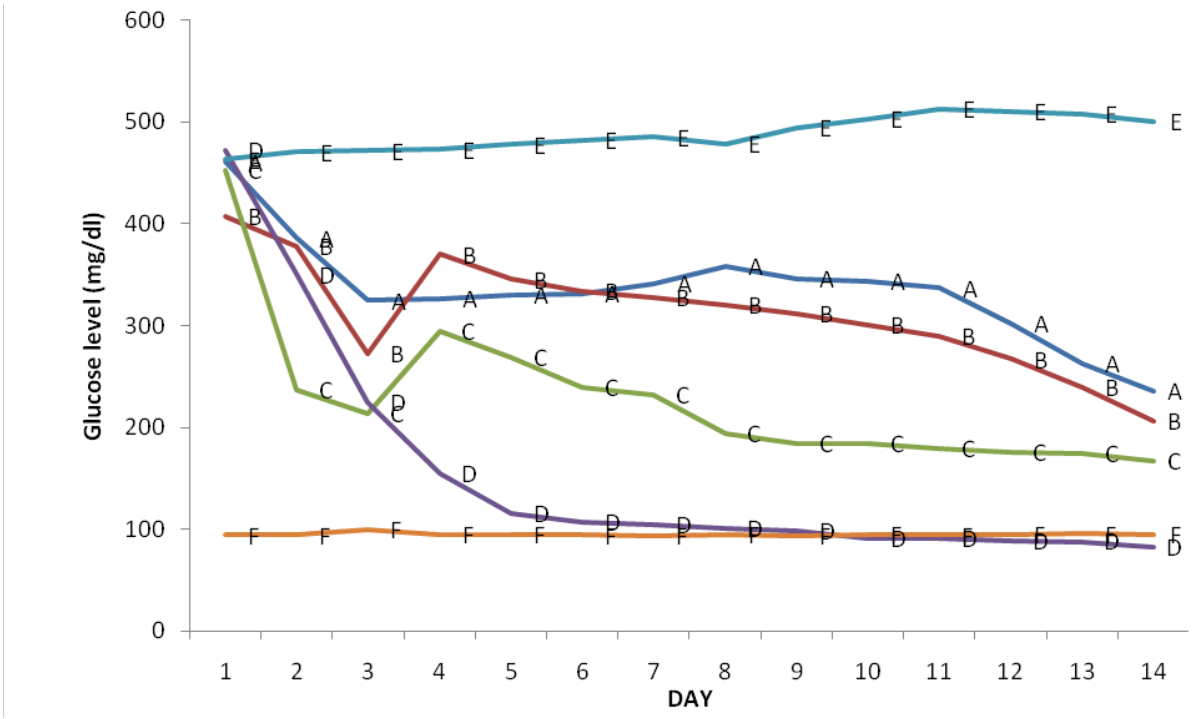

Figure 1: Glucose index in alloxan-induced diabetic rats treated with *Buchholzia coricea* extract and vildagliptin for 14 days

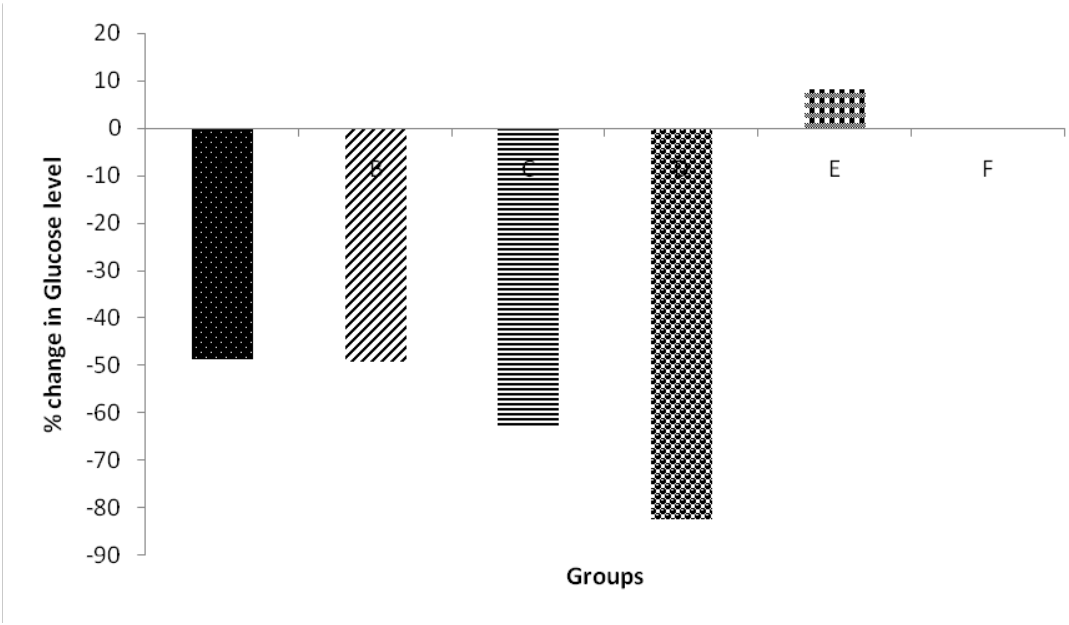

Figure 2: Percentage change in glucose levels of animals treated with *Buchholzia coricea* extract and vildagliptin within the fourteen day period of administration

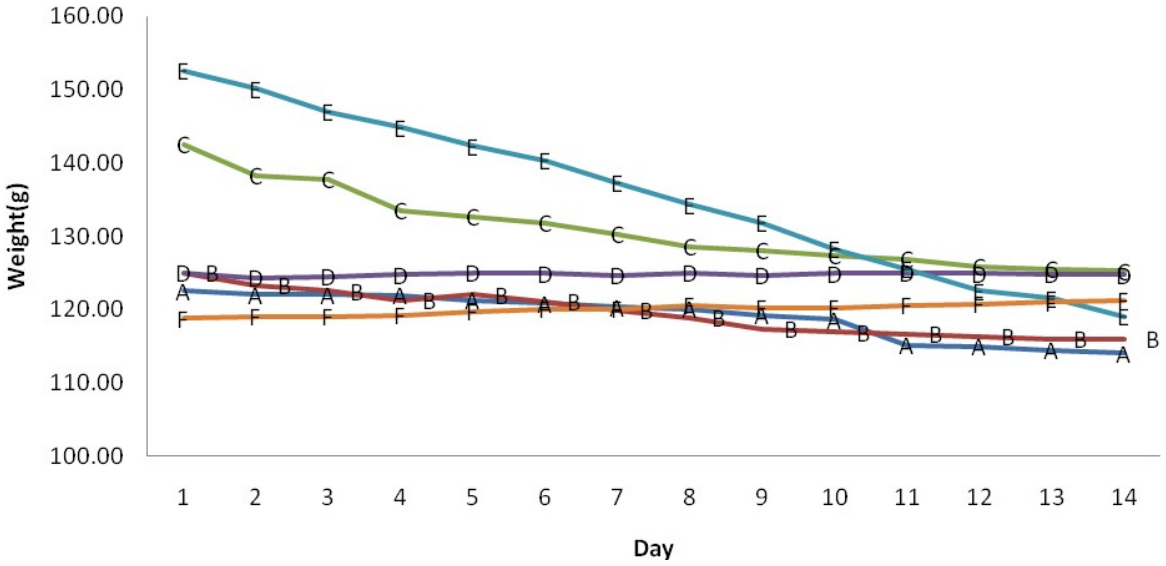

Figure 3: Body weights of alloxan-induced diabetic albino rats treated with *B. coriacea* ethanol seed-extract and Vildagliptin

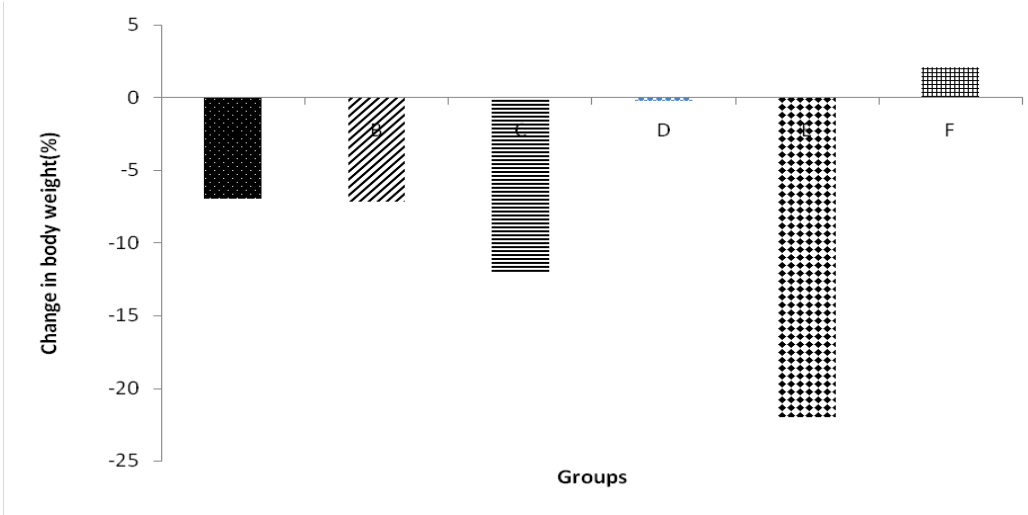

Figure 4: Percentage change in body weights of alloxan-induced diabetic rats treated with *B. coriacea* ethanol seed-extract and vildagliptin

Key:

A-Group that received *B. coriacea* ethanol seed-extract 100mg/kg body weight
B-Group that received *B. coriacea* ethanol seed-extract 200mg/kg body weight
C-Group that received *B. coriacea* ethanol seed-extract 400mg/kg body weight
D-Group that received vildagliptin 1.43mg/kg body weight
E-Group that received alloxan without treatment
F-Normal control

DISCUSSION

Diabetic rats treated with *B. coriacea* ethanol seed-extract and vildagliptin significantly ($p<0.05$) reduced blood glucose levels as shown in Figures 1 and 2. The reduction in plasma glucose levels was dose dependent. Animals in the groups treated with vildagliptin at 1.43mg/kg and *B. coriacea* seed extract at the dose of 400mg/kg gave over 60% reductions in glucose levels. Okoye *et al.* (2012) reported a reduction in glucose levels by 11.30% after 4 hours of administration of methanol seed-extract of *B. coriacea* at 400mg/kg body weight. Adisa *et al*. (2011) also recorded 55% reduction in plasma glucose levels in the diabetic rats after 10 days. More so, Nwaehujor *et al.* (2012) reported that treatment with 150, 300 and 600 mg/kg body weight of methanol extract of *B. coriacea* seed significantly ($p<0.05$) induced over 50% reduction in plasma glucose levels for all the groups treated at the stipulated doses. Lenka *et al.* (2016) also reported a significant reduction in plasma glucose levels in alloxan induced diabetic rats treated with *B. coriacea* seed-extract.

More so, the results showed that the body weights decreased significantly ($p<0.05$) in the groups treated with *B. coriacea* extract and there was no significant ($p>0.05$) change in body weights in vildagliptin group as

shown in Figures 3 and 4 respectively. Abdella *et al.* (2014) reported that 800 mg/kg body weight of aqueous extract of *Balanites aegypticea* fruits significantly ($p \leq 0.05$) increased body weight ($p \leq 0.05$) compared to the diabetic control. More so, Kulkarni, Y.A. and Veeranjaneyulu, A. (2013) reported that aqueous extract of Gmelina arborea also reduced loss of body weight in experimentally induced diabetic rats. According to Luc and Andre (2015), diabetes and overweight are intrinsically linked, overweight contributing to the progression of diabetes and the associated cardiovascular risks. Weight gain has been shown to worsen diabetic control by causing increased insulin resistance while weight reduction may have a reversal effect (Mark *et al.,* 2005). Even though weight loss is an important component of diabetes management, it is not usually easy to achieve alongside effective plasma glucose reduction. Therefore weight reduction by the extract could be seen as a desirable occurrence that can improve glucose control in diabetic subjects.

In conclusion, both *B. coriacea* ethanol seed-extract (at higher doses) and vildagliptin effectively reduced plasma glucose levels in alloxan-induced diabetic rats. However, there was a reduction in body weights in diabetic animals treated with the extract.

REFERENCES

Abdella, E. A. B., Waleed, H. A., Imran, S., Fatimah, A. B., Hanouf, S. B., and Omar, M. I. (2014). Eldeen (2014).The hypoglycemic effect of the aqueous extract of the fruits of *Balanites aegypticea* in Alloxan-induced diabetic rats. *Pharmacognosy Research*, **6**(1):1-5

[1] Adisa, R. A., Choudharyb, M. I. and Olorunsogo, O. O. (2011). Hypoglycemic activity of *Buchholzia coriacea* (Capparaceae) seeds in streptozotocin-induced diabetic rats and mice. *Experimental and Toxicologic Pathology,* **63**(7-8): 619-625

[2] Adjanohoun, J. E., Aboubakar, N., Dramane, K., Ebot, M. E., Ekpere, J. A., Enoworock, E. G., Focho, D., Gbile, Z. O., Kamanyi, A., Kamsu, K. J., Keita, A., Mbenkum, T., Mbi, C. N., Mbiele, A. C., Mbome, J. C., Muberu, N. K., Nancy, W. L., Kongmeneck, B., Satabie, B., Sowora, A., Tamze, V. and Wirmum, C. K. (1996). Organization of African Unity; Scientific, Technical and Research Commission, editor.

Traditional Medicine and Pharmacopoeia: Contribution to ethno botanical and floristic studies in Cameroon.

[3] Ahrén, B., Landin-Olsson, M., Jansson, P. A., Svensson, M., Holmes, D. and Schweizer, A. (2004). Inhibition of dipeptidyl peptidase-4 reduces glycemia, sustains insulin levels, and reduces glucagon levels in type 2 diabetes. *The Journal of Clinical Endocrinology and Metabolism,* **89** (5): 2078–2084

[4] Ahrén, B., and Pacini, G. (2005). Islet adaptation to insulin resistance: mechanisms and implications for intervention. *Diabetes Obesity and Metabolism*, **7**: 2–8.

[5] Ajaiyeoba, E. O., Onocha, P. A. and Olanrewaju, O. T. (2001). *In vitro* anti-helminthic properties of *Buchholzia coriacea* and *Gynandropsis gynandra*. *Journal of Pharmaceutical Biology*, **39**: 217–220.

[6] Dhanabal, S. P., Raja, M. K., Ramanathan, M. and Suresh, B. (2007). Hypoglycemic activity of *Nymphaea stellata* leaves ethanolic extract in alloxan induced diabetic rats. *Fitoterapia*, **78**:288–291.

[7] Edgar, J., DaSilva, Elias, B. and Adnan, B. (2002). Biotechnology and the developing world. *Electronic Journal of Biotechnology,* **5** (1):10-15.

[8] Ezeigbo, I. I. (2010). Anti-diabetic potential of methanolic leaf extracts of *Icacina trichantha* in alloxan-diabetic mice. *International Journal of Diabetes in Developing Countries,* **30**:150–152.

[9] Ezekiel, O. O. and Onyeoziri, N. F. (2009). Preliminary studies on the antimicrobial properties of *Buccholzia coriacea*. *African Journal of Biotechnology*, **8**(3): 472-474.

[10] Hemingway, C. A. (2004). Plants and People. *Edible plant Journal*, 1: 72-78 International Diabetes Federation (2006). Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia. *Diabetes Atlas*, **3**: 3-15.

[11] International Diabetes Federation (2006). Definition and diagnosis of diabetes mellitus and intermediate

hyperglycemia.*Diabetes Atlas*,**3**: 3-15.

[12] Keay , R. W. J. (1989). Trees of Nigeria, Clarendon press, Oxford . 42-44.

[13] King, H., Aubert, R. E.and Herman, W. H. (1998). Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. *Diabetes Care,* **21**: 1414–1431.

[14] Knip, M., Veijola, R., Virtanen, S. M., Hyöty, H., Vaarala, O. and Akerblom, H. K. (2005). Environmental Triggers and Determinants of Type 1 Diabetes. *Diabetes,* **54**: 125–136.

[15] Kulkarni, Y.A. and Veeranjaneyulu, A. (2013).Effects of Gmelina arborea extract on experimentally induced diabetes. Asian Pacific Journal of Tropical Medicine, **6**(8): 602-608.

[16] Lenka, J. L., Luka, Carol, D. and Larfa, S. N. (2016). The effect of aqueous extract of *Buchholzia coriacea* seeds on some biochemical parameters in normal and alloxan-induced diabetic rats. *International Journal of Biochemistry Research and Review,* **11** (1): 1-10.

[17] Lloret-Linares, C., Greenfield, J.R.and Czernichow, S.(2008).Effect of weight-reducing agents on glycaemic parameters and progression to Type 2 diabetes: a review. *Diabetic Medicine*, **25**(10):1142-1150.

[18] Luc, V. G. and Andre, S. (2015). Weight management in type 2 diabetes: current and emerging approaches to treatment. *Diabetes Care,* **38** (6): 1161-1172.

[19] Mark, A. P., Alex, I. K., Cara, B. E., Linda, V. H., Martha, L. S., David, R. J. Jr., David, S. L. (2005). Fast-food habits, weight gain, and insulin resistance (the CARDIA study): 15-year prospective analysis. *Lancet*; **365**: 36–42

[20] Mbata, T. I., Duru, C.M. and Onwumelu, H. A. (2009). Antibacterial activity of crude seed extract of *Buccholzia coriacea* E. on some pathogenic bacterials. *Journal of Developmental Biology and Tissue Engineering*, **1**(1):1-5.

[21] Mentlein, R., Gallwitz, B. and Schmidt, W. E. (1993). Dipeptidyl-

peptidase IV hydrolyses gastric inhibitory polypeptide, glucagon-like peptide-1(7-36)amide, peptide histidine methionine and is responsible for their degradation in human serum. *European Journal of Biochemistry / FEBS,* **214** (3): 829–835.

[22] Metzger, B. E. and Coustan, D. R. (1998). Proceedings of the Fourth International Work-shop-Conference on Gestational Diabetes Mellitus. *Diabetes Care,* **21** (2): 1–167.

[23] Müller, W. *A.,* Faloona, G. R., Aguilar-Parada, E. and Unger, R. H. (1970). Abnormal alpha-cell function in diabetes. Response to carbohydrate and protein ingestion. *New England Journal of Medicine*, **283**: 109–115.

[24] Nwaehujor, C. O.; Ode, O. J., Nwinyi, F. C. and Udeh, N. E. (2012). Effects of Methanol Extract of Buchholzia coriacea Fruit in Streptozotocin-induced Diabetic Rats. *Journal of Pharmacology & Toxicology*, **7**(4):181

[25] Okoli, B. J., Okere, O. S. and Adeyemo, S. O. (2010). The antiplasmodic activity of *Buccholzia coriacea*. *Journal of Medical and Applied Biosciences*, **2**: 21-29.

[26] Okoye, T. C., Akah, P. A, Ilogu, C.L., Ezike, A. C. and Onyeto, C. A. (2012). Anti-diabetic effects of methanol extract of the seeds of *Buchholzia coriacea* and its synergistic effects with metformin. *Asian Journal of Biomedical and Pharmaceutical Sciences,* **2**(12):32-36.

[27] Pittler, M., Abbot, N. C., Harkness, E. F. and Ernest, E. (2000). Location bias in controlled clinical trials of complementary/alternative therapies. *International Journal of Epidemiology,* **53** (5): 485–489

[28] Srinivasan K. 2005. Spices as influencers of body metabolism:an overview of three decades of research. *Food Research International,* **38**:77–86.

[29] Weyer, C., Bogardus, C., Mott, D. M. and Pratley, R.E.(1999). The natural history of insulin secretory dysfunction and insulin resistance in the pathogenesis of type 2 diabetes mellitus.*Journal of Clinical Investigation,* **104**: 787–794.