International Scholars Journals

International Journal of Medicinal Plants Research ISSN: 2169-303X Vol. 5 (1), pp. 173-177, January, 2016. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Full Length Research Paper

Hypoglycemic effect of *Phragmanthera incana* (klotzsch) on alloxan- induced diabetic albino rats

***[1, 2]Ogunmefun, O.T., [2]Fasola, T.R., [3]Saba, A.B, [3]Oridupa, O.A. and [4]Adarabioyo, M.I.**

[1]Department of Biological Sciences, College of Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.
[2]Department of Botany, Faculty of Science, University of Ibadan, Ibadan, Nigeria.
[3]Department of Physiology, Biochemistry and Pharmacology, Faculty of Veterinary Medicine, University of Ibadan, Ibadan, Nigeria.
[4]Department of Statistics, College of Sciences, Afe Babalola University, Ado-Ekiti, Nigeria.

Accepted 23 July, 2014

Anti-diabetic effect of *Phragmanthera incana*, a mistletoe species growing on *Theobroma cacao* (Cocoa) and *Cola nitida (Kolanut)* were investigated based on its ethnomedicinal claims for treatment and management of diabetes in Nigeria. Diabetes was induced by intraperitoneal injection of alloxan (100mg/kg) in albino rats. After 4 days monitoring, rats with RBS of ≥150mg/dl were considered diabetic and included in the study. Eight groups of diabetic rats (n=5), and a ninth group of non-diabetic rats were used for the study. Three groups of diabetic rats were assigned to each extract and administered doses of 200, 400 or 800mg/kg. One group was administered with glibenclamide and the eighth group was left untreated. RBS were monitoring within 24 hours and days 3, 7, 10 and 14 post-administration of extracts. The extracts reduced RBS within 1 hour post-administration of the extract, and through the course of the experiment. Twenty four hours post-administration of extracts, rats administered 800mg/kg exhibited the lowest RBS, but in the overall, 400mg/kg dose achieved the best control of blood glucose levels. The extracts achieved a more significant control of blood glucose levels than glibenclamide. This study justifies the use of this plant in ethnomedicine for management of diabetes mellitus.

Key words: *Phragmanthera incana*, *theobroma cacao*, *cola nitida*, alloxan, diabetes.

INTRODUCTION

Mistletoe is a common name for various parasitic plants belonging mostly to Loranthaceae family (Watson, 2001; Judd *et al.*, 2002). Ancient Europeans believed that the mistletoe plant held magical powers to bestow life and fertility, bring peace, and protect against disease. Northern Europeans associated the plant with Norse goddess of love, Freya, and developed the custom of kissing underneath mistletoe branches. Christians incorporated this custom into their Christmas celebrations, and kissing under a mistletoe branch eventually became a part of secular Christmas tradition (Drury, 1987). Mistletoe is especially interesting botanically because it is a hemiparasite (partial parasite). Mistletoe is also capable of growing on its own; like other plants as it can produce its own food by photosynthesis. However, it is more commonly found growing as a parasitic plant (Runyon *et al.*, 2009).

Mistletoe is used mainly in Europe as a treatment for cancer (Kovacs, 2004; Augustin *et al.*, 2005). While American mistletoe is toxic, European mistletoe is considered to have medicinal properties till today (Krenzelok *et al.*, 1997). Currently, it is best used as an adjuvant therapy with cancer chemotherapy or radiotherapy (Mengs *et al.*, 2002; Bock *et al.*, 2004). Mistletoe has been used in medicine to prove much of its older frame as “all healer”. The white-berried mistletoe (*Viscum album*) has been documented as a traditional treatment for diabetes and high blood pressure.

Mistletoe extracts represent the most unorthodox oncology therapy in Germany (Bock *et al.*, 2004; Orhan *et al.*, 2005). *V. album* has been also reported to reduce heart rate, stimulate the immune system, relax spasms and exert sedative, diuretic and anti-cancer effects (Bown, 1995).

*Corresponding author: E-mail: bensaba2011@hotmail.com

A tea prepared from leaves of mistletoe is used traditionally to treat diabetes in the West Indies. This treatment has been shown also to relieve the diabetic symptoms of severely hyperglycaemic streptozotocin-diabetic mice, including polydipsia, hyperphagia and body weight loss (Swanston-Flatt *et al.*, 1989). In Nigeria, the Hausa and Fulani tribes of Northern Nigeria use mistletoe in the treatment of cancers and inflammations. (Abubakar *et al.*, 2007). The African mistletoe, *Loranthus bengwensis* L. (Loranthaceae), has been widely used in Nigerian folk medicine to treat Diabetes mellitus (Obatomi *et al.*, 1994).

This present study was based on African mistletoe, *Phragmanthera incana*, a woody parasitic shrub, which stems up to 2m long; of secondary jungle and bush savanna areas. Young parts and perianth are more or less densely covered with brown hairs with red berries. The plant is very variable in the shape and size of the flowers and leaves (Burkill, 1985). Phragmanthin, a single peptide with low molecular weight (10.7kD) and haemaglutinin activity was isolated and purified to homogeneity from fresh leaves of *P. incana* (Fasanu and Oyedapo, 2008). Metabolic studies of phragmanthin on Sprague – Dawley rats revealed that it caused significant reduction in the levels of plasma inorganic phosphate, haemoglobin, activities of L- alanine aminotransferase and alkaline phosphatase, muscle glycogen and blood sugar. Though, a slight elevation of the levels of plasma L – aspartate aminotransferase activity and creatinine was exhibited (Fasanu and Oyedapo, 2008). However, the effect of this mistletoe on diabetes is yet to be investigated. This study was therefore aimed at evaluating the probable changes in fasting and or random blood glucose (Random Blood Sugar – RBS) levels of diabetic albino rats administered with the methanol extract of *P. incana* harvested from cocoa or kolanut trees.

MATERIALS AND METHODS

Plant Sample Collection

Phragmanthera incana (mistletoe) were harvested from two plant hosts [*Theobroma cacao* (Cocoa) and *Cola nitida (Kolanut)*] in a forest at Alesan Obolode, Owo metropolis, Nigeria. Authentication of the mistletoe species was carried out at the Forestry Research Institute of Nigeria with Forest Herbarium Index 108925. A voucher specimen was submitted at the Department of Botany, University of Ibadan Herbarium.

Plant Sample Extraction

The samples were washed, air dried and ground to powder and kept dry in an air-tight container. Cold extraction method for 72 hours with methanol was used and were concentrated using rotary evaporator. The concentrated extracts were further dried on water bath at a very low temperature of about 40^0 C to remove all solvents.

Experimental Animals

Albino rats were obtained from and housed at Experimental Animal Unit of the Faculty of Veterinary Medicine of the University of Ibadan. The rats were allowed access to water and pelletized rat feed *ad libitum.* The rats were humanely handled according to the Animal Use Ethical Guide stated by the Faculty of Veterinary Medicine Committee on animal right and uses.

Antidiabetes Studies

Diabetes was induced in albino rats weighing between 120-200g with alloxan (100mg/kg). Following an overnight fast, fasting blood sugar levels (FBS) of the rats were measured using Accu-check glucometer and diabetes was induced by intraperitoneal injection of alloxan. The rats were monitored for 4days and rats with blood glucose level of ≥150mg/dl were considered diabetic and included in the study. Forty diabetic rats were randomly and equally divided into eight groups. Three groups were designated for treatment with the graded doses of *P. incana* extract harvested from Cocoa tree, 3 groups were treated with *P. incana* extract harvested from Kolanut tree, one group was treated with glibenclamide, a standard anti-diabetic drug, and the 8^{th} group of diabetic rats was left untreated. A 9^{th} group of non-diabetic and untreated rats were included as control for the study. Treatment with methanol extracts of *P. incana* at the doses of 200mg/kg, 400mg/kg or 800mg/kg commenced four days post induction of diabetes with alloxan. Thereafter, random blood sugar levels (RBS) of all the rats were measured post-administration of the extracts over a period of twenty-four hours, beginning at 1, 3, 6, 12 and 24 hours, and on days 1,3,7,10 and 14 post-administration of the extract.

Statistical Analysis

Data were presented as mean and the standard error of mean of the results from this study. The results were analyzed by paired sample t-test descriptive statistical mode of analysis using the Statistical Package for Social Sciences (SPSS 15) to compare the differences in the mean values of the different rat groups.

RESULTS

All the doses of the extracts of *P. incana* reduced blood glucose levels within the first hour post-administration of

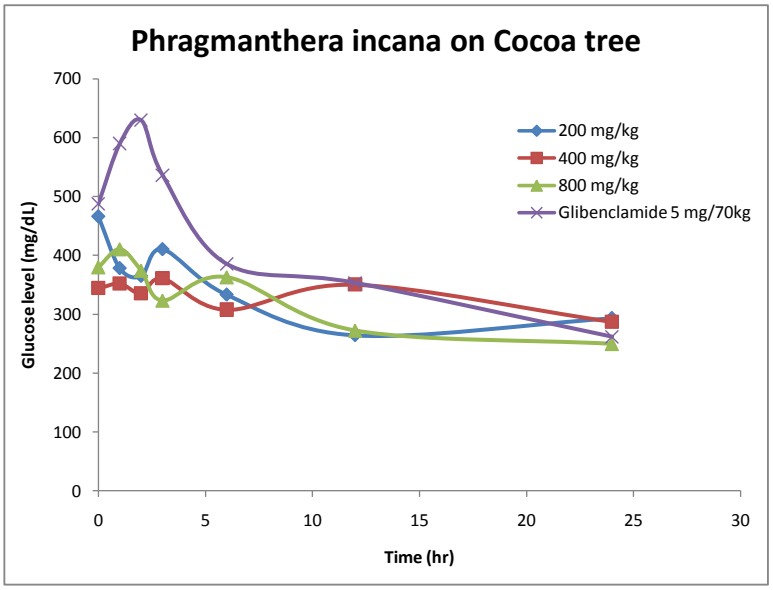

Figure 1. Twenty four hours monitoring of blood glucose levels (mg/dL) of alloxan-induced diabetic rats administered with methanol extract of *Phragmanthera incana* harvested from *Theobroma cacao* (Cocoa).

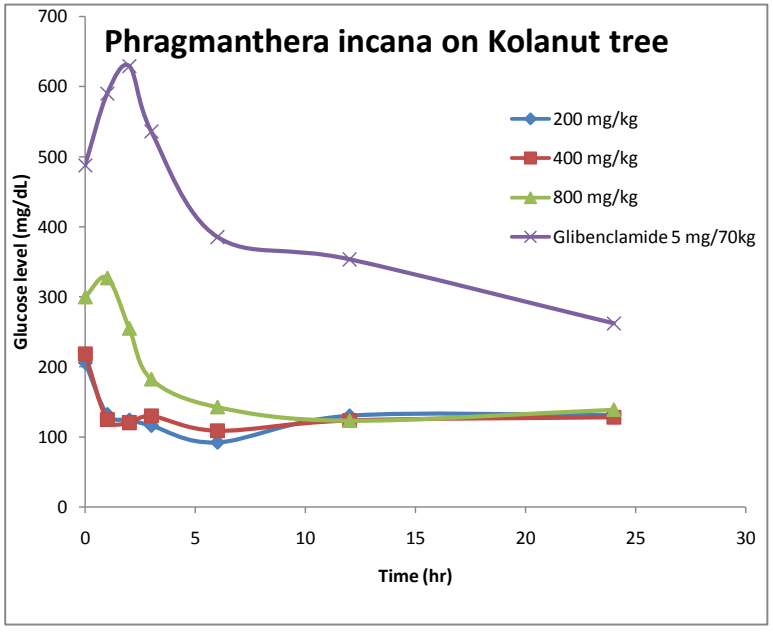

Figure 2. Twenty four hours monitoring of blood glucose levels (mg/dL) of alloxan-induced diabetic rats administered with methanol extract of *Phragmanthera incana* harvested from *Cola nitida* (Kolanut).

the extracts (Figure 1 & 2). There was a significant reduction in the blood glucose levels of rats administered with the different doses of *P. incana* extract harvested from Cocoa compared to the untreated diabetic rats. Although, the different doses of the extract did not cause significant reduction compared within the doses, the reductions caused were statistically significant compared to glibenclamide, particularly within 12hours post-administration of the extract (Figure 1).

P. incana extract harvested from Kolanut tree significantly reduced the blood glucose levels of rats compared to the untreated diabetic rats. Rats administered with the extract had significantly lower blood glucose levels compared to rats administered with glibenclamide. There was an insignificant difference between the blood glucose of rats administered with the extract and the non-diabetic rats at the end of the study. At the end of 24 hours, the highest dose of the extract (800mg/kg) had the most profound

Table 1. Random blood sugar (RBS) levels of rats administered with *Phragmanthera incana* extract harvested from *Theobroma cacao* (Cocoa).

	0 hr	Day 1	Day 3	Day 7	Day 10	Day 14
200mg/kg	466.2±57.92	248.8±57.23	309.8±48.38	158.8±18.81	185.2±17.52	130.8±62.08
400mg/kg	344.2±44.56	294.4±27.52	183.0±36.8	129.8±64.56	125.0±36.00	98.2±24.64
800mg/kg	379.8±52.56	214.8±40.96	199.6±28.24	191.4±29.52	197.2±61.36	175.2±17.84
Glibenclamide	429.7±13.11	214.0±3.33	239.7±6.44	261.7±20.22	206.3±37.56	159±58.00
Diabetic Ctrl	308.8±46.16	363.6±44.88	399.2±72.96	397.2±64.56	402.6±62.08	417.2±54.56
Non-Diabetic	81.2±20.96	115.0±23.2	110.0±12.4	92.4±4.88	97.8±5.92	81.4±10.32

Table 2. Random blood sugar (RBS) levels of rats administered with *Phragmanthera incana* extract harvested from *Cola nitida* (Kolanut).

	0 hr	Day 1	Day 3	Day 7	Day 10	Day 14
200mg/kg	174.4±16.48	138.6±22.32	121.0±6.4	106.6±8.32	97.4±16.96	99.6±11.2
400mg/kg	218.6±80.32	141.6±32.32	120.8±8.56	113.0±25.2	90.0±21.2	78.8±14.56
800mg/kg	299.8±59.36	286.0±10.4	264.4±6.24	248.8±17.68	151.8±23.76	127.2±10.16
Glibenclamide	429.7±13.11	214.0±3.33	239.7±6.44	261.7±20.22	206.3±37.56	159.0±58.00
Diabetic Ctrl	308.8±46.16	363.6±44.88	399.2±72.96	397.2±64.56	402.6±62.08	417.2±54.56
Non-Diabetic	81.2±20.96	115.0±23.2	110.0±12.4	92.4±4.88	97.8±5.92	81.4±10.32

effect on the blood glucose, but 400mg/ml of each of the extract had a better overall hypoglycemic effect as observed in the course of monitoring on days 3, 7 ,10 and 14 (Table 1 & 2).

DISCUSSIONS

Methanol extracts of *Phragmanthera incana* harvested from host plants *Theobroma cacao* (Cocoa) and C*ola nitida* (kolanut) both exhibited significant hypoglycemic effects in the alloxan-induced diabetic rats. The extracts had hypoglycemic effects within 1 hour post-administration of the extract, which was sustained through the course of the experiment. The hypoglycemic effect of the extracts was comparable to the standard anti-diabetic drug, glibenclamide. The extracts at the dose of 800mg/kg exhibited the most profound hypoglycemic effect 24 hours post-administration of the extracts, but the extracts at 400mg/kg exhibited the best control of the blood glucose levels through the course of the study. *P. incana* harvested from kolanut exhibited more hypoglycemic effect compared to that harvested from cocoa. This correlated well with the phytochemical screening of the mistletoes growing on the two plant hosts which showed differences in their phytochemical profiles (Ogunmefun *et al.*, 2013). The two extracts showed consistent and sustained lowering of the blood glucose levels throughout the 14-day period of observation, despite the single dose of the extract administered on day 0.

In this study, the rats administered with the extracts of *P. incana* exhibited a better controlled blood glucose levels compared to rats administered with glibenclamide. Diabetes mellitus was induced in all the rats by intraperitoneal injection of alloxan, a toxic glucose analogue proven to induce an insulin-dependent diabetes when administered to rodents and many other animal species by selectively destroying insulin-producing β-cells of the Islet of Langerhans in the pancreas (Lenzen, 2008). It has been successfully used to experimentally induce diabetes and reversal of damage can be determined by monitoring of blood glucose levels. Random and or fasting blood glucose levels are essential parameters for determination of diabetes status of a patient and monitoring of response to interventions employed for management of diabetes mellitus. Response to anti-diabetic drugs is determined by the ability of the drug to lower and maintain normal blood glucose levels. Blood levels need to be properly controlled in diabetic subject to prevent development of its associated complications such as eye, kidney and or heart disease, as well as nerve damage, amongst other complications (Adler *et al.*, 2003; Boulton *et al*., 2005; Boyle, 2007; Keenan *et al.*, 2007).

This study has demonstrated the anti-diabetic effect of *Phragmanthera incana* species harvested from different plant hosts, confirming the ethno traditional use of the plant for management of diabetes mellitus. Another African mistletoe *Loranthus bengwensis* L. (Family: Loranthaceae) that have been proven to possess anti-diabetic effect. This mistletoe significantly decreased

blood glucose levels of streptozocin-induced diabetic rats monitored for 28 days. The researchers also reported a variation in the anti-diabetic property of the mistletoes from different plant hosts (Obatomi *et al.*, 1994). Recently, Osadolor and Ojewe (2008) investigated the hypoglycemic effect of the aqueous extract of *L. bengwensis* in normal (non-diabetic) rats and reported that it significantly lowered blood glucose levels.

Other medicinal plants shown to possess anti-diabetic property include *Vernonia amygdalina* (Nwaoguikpe, 2010) which lowered blood glucose levels in alloxan-induced diabetic rats. Atangwho *et al.* (2013) further 999evaluated the anti-diabetic effect of fractions of the extract in relation to their antioxidant effect. Oyagbemi *et al.* (2010) reported the antidiabetic property of *Cnidoscolus aconitifolius* administered to alloxan-induced diabetic rats. The anti-diabetic effect of *Garcinia kola* was also reported by Udenze *et al.* (2012) in alloxan-induced diabetic rats and Adaramoye (2012) reported the anti-diabetic effect of kolaviron, a biflavonoid isolated from *G. kola* in streptozocin- induced diabetic rats.

In conclusion, *P. incana* growing on host plants *Theobroma cacao* (Cocoa) and C*ola nitida* (kolanut) are confirmed to have anti-diabetic property and further studies are recommended to explore the bioactive principle responsible for the hypoglycemic effect of *P. incana* with probable establishment of the mechanism(s) of glucose uptake involved.

REFERENCES

Abubakar MS, Musa AM, Ahmed A, Hussaini IM (2007). The perception and practice of traditional medicine in the treatment of cancers and inflammations by the Hausa and Fulani tribe of Northern Nigeria. J. Ethnopharmacol. 3(3): 625–629.

Adaramoye OA (2012). Antidiabetic effect of kolaviron, a biflavonoid complex isolated from *Garcinia kola* seeds, in Wistar rats. Afr. Health Sci. 12(4): 498–506.

Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR (2003). Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney Int. 63: 225-232.

Atangwho IJ, Egbung GE, Ahmad M, Yam MF, Asmawi MZ (2013). Antioxidant versus anti-diabetic properties of leaves from *Vernonia amygdalina* Del. growing in Malaysia. Food Chem. 15; 141(4): 3428-34.

Augustin M, Bock PR, Hanisch J, Karasmann M, Schneider B (2005). Safety and efficacy of the long-term adjuvant treatment of primary intermediate- to high-risk malignant melanoma (UICC/AJCC stage II and III) with a standardized fermented European mistletoe (*Viscum album* L.) extract. Results from a multicenter, comparative, epidemiological cohort study in Germany and Switzerland. Arzneim. Forsch. 55: 38-49.

Bock PR, Friedel WE, Hanisch J, Karasmann M, Schneider B (2004). Efficacy and safety of long-term complementary treatment with standardized European mistletoe extract (*Viscum album* L.) in addition to the conventional adjuvant oncologic therapy in patients with primary non-metastasized mammary carcinoma. Results of a multi-center, comparative, epidemiological cohort study in Germany and Switzerland (in German). Arzneim. Forsch. 54: 456-66.

Boulton AJ, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R, Malik RA, Maser RE, Sosenko JM, Ziegler D (2005). Diabetic neuropathies: a statement by the American Diabetes Association. Diabetes Care 28: 956-962.

Bown D (1995). The Royal Horticultural Society Encyclopaedia of Herbs and their Uses. London: Dorling Kindersley Ltd.

Boyle PJ (2007). Diabetes mellitus and macrovascular disease: mechanisms and mediators. Am. J. Med. 120: S12-S17.

Burkill HM (1985). The Useful Plants of West Tropical Africa Vol 3.

Drury S (1987). Customs and beliefs associated with Christmas Evergreens: A preliminary survey. Folklore 98(2): 194–199.

Fasanu PO, Oyedapo OO (2008). Phragmanthin-peptide from fresh leaves of African mistletoe (*Phragmanthera incana*): purification and metabolic activities. In: Phytopharmacology and Therapeutic Values: Recent progress in medicinal plants (Singh VK, Govil JN, editors) 19(1): 39- 47.

Judd WS, Campbell CS, Kellogg EA, Stevens PF, Donaghue MJ (2002). Plant systematics: a phylogenetic approach. Sinauer Associates, Inc., Sunderland Massachusetts, USA. ISBN 0-87893-403-0

Keenan HA, Costacou T, Sun JK, Doria A, Cavellerano J, Coney J, Orchard TJ, Aiello LP, King GL (2007). Clinical factors associated with resistance to microvascular complications in diabetic patients of extreme disease duration: the 50-year medalist study. Diabet. Care 30: 1995-1997.

Kovacs E (2004). Effects of *Viscum album* extract therapy in patients with cancer: relation with interleukin-6, soluble interleukin-6 receptor, and soluble gp130. J. Altern. Complement Med., 10: 241-6.

Krenzelok EP, Jacobsen TD, Aronis J (1997). American mistletoe exposures. Am. J. Emerg. Med., 15: 516-520.

Lenzen S (2008). The Mechanisms of Alloxan- and Streptozotocin-induced Diabetes. Diabetologia 51(2): 216–226.

Mengs U, Gothel D, Leng-Peschlow E (2002). Mistletoe extracts standardized to mistletoe lectins in oncology: review on current status of preclinical research. Anticancer Res., 22:1399-407.

Nwaoguikpe RN (2010). The effect of extract of bitter leaf (*Vernonia amygdalina*) on blood glucose levels of diabetic rats. Int. J. Biol. Chem. Sci., 4(3): 721-729.

Obatomi DK, Bikomo EO, Temple VJ (1994). Antidiabetic

properties of the African mistletoe in streptozotocin-induced diabetic rats. J. Ethnopharmacol., 43(1):13–17.
Ogunmefun OT, Fasola TR, Saba AB, Oridupa OA (2013). The ethnobotanical, phytochemical and mineral analyses of *Phragmanthera Incana* (Klotzsch), A species of mistletoe growing on three plant hosts in South-Western Nigeria. Int. J. Biomed. Sci., 9(1): 33-40.
Orhan DD, Aslan M, Sendogdu N, Ergun F, Yesilada E (2005). Evaluation of the hypoglycemic effect and antioxidant activity of three *Viscum album* subspecies (European mistletoe) in streptozotocin-diabetic rats. J. Ethnopharmacol., 98: 95-102.
Osadolor HB, Ojewe DD (2008): Hypoglycemic Effect of Aqueous Extract of African Mistletoe (Loranthus bengwensis) Leaves in Normal Rabbits. Cont. J. Appl. Sci., 3: 21-24.
Oyagbemi AA, Odetola AA, Azeez OI (2010). Antidiabetic properties of ethanolic extract of *Cnidoscolus aconitifolius* on alloxan induced diabetes mellitus in rats. Afr. J. Med. Med. Sci., 39 Suppl: 171-178.
Runyon J, Tooker J, Mescher M, De Moraes C (2009). Parasitic plants in agriculture: Chemical ecology of germination and host-plant location as targets for sustainable control: A review. Sus. Agric. Rev., 1: 123-136.
Swanston-Flatt SK, Day C, Bailey CJ, Flatt PR (1989). Evaluation of traditional plant treatments for diabetes: studies in streptozotocin diabetic mice. Acta Diabetol. Lat. 26: 51–55.
Udenze ECC, Braide VB, Okwesilieze CN, Akuodor GC (2012). Pharmacological effects of *Garcinia kola* seed powder on blood sugar, lipid profile and atherogenic index of alloxan-induced diabetes in rats. Pharmacologia 3(12): 693-699.
Watson D (2001). Mistletoe: a keystone resource in forests and woodlands worldwide. Ann. Rev. Ecol. Sys., 32: 219-249.