ASSESSMENT OF ANTIDIABETIC ACTIVITY OF COMBINED ETHANOLIC LEAF EXTRACTS FROM FOUR MEDICINAL PLANTS: OCIMUM GRATISSIMUM, CARICA PAPAYA, CYMBOPOGON CITRATUS AND MORINGA OLEIFERA IN DEXAMETHASONE-INDUCED DIABETIC WISTAR RATS

Olawunmi, Muibat Omowunmi; Taiwo, Adebimpe Abidemi and Akindele, Oluwayemisi
Department of Science Laboratory Technology, Chemistry/Biochemistry unit
Moshood Abiola Polytechnic, Abeokuta, Ogun State, Nigeria.
Corresponding author: olawunmi.muibat@mapoly.edu.ng

ABSTRACT

Diabetes mellitus is a group of metabolic disorders characterised by absolute lack of or deficiency of insulin leading to hyperglycemia, glycosuria and hyperlipaemia. Polyherbal therapy is said to be a current pharmacological principle having the advantage of producing maximum therapeutic efficacy with minimum side effects. The objective of the study is to investigate the antidiabetic activity of combined ethanolic (AlcE) extracts of leaf of *Moringa oleifera*, *Ocimum gratissimum*, *Cymbopogon citratus* and *Carica papaya* in normal and diabetic induced rats. The plants were tested for their phytochemical constituents and it was observed that the entire plants extract has Saponin, Flavonoid which was not significantly present in *C. citratus* and Tannin which was not significantly present in *O.gratissimum* and *M.oleifera.* Thirty-six (36) Wistar rats were grouped equally into six groups. Group I and II served as normal control group (NCG) and Diabetic control groups (DCG) respectively, group III-VI serves as the diabetic treatment (DTG) groups. DCG and DTG (Group II-VI) were induced with diabetics by injection of dexamethasone in normal saline (10 mg/kg, i.p) for 10 days. The DCG receive metformin (100mg/kg, i.p) and DTG's received the combined extracts at different concentration of 200, 300, 400 and 500mg/kg body weight orally for 14 days. Thereafter, the animals were sacrificed and blood was collected for serum glucose. Changes in animal weight were also measured within the period. From the results it was observed that DCG and DTG had significant increase in body weight ($P<0.005$), DTG having percentage increase of 5.56%, 4.67%, 6.82%, 5.22% respectively which were slightly higher than the DCG (4.20%). The combined extract, significantly ($P<0.005$) decreased the blood glucose level. This result thus showed that combined AlcE of the above mentioned plants could be used in treatment of diabetics.

KEYWORDS: Anti-Diabetics, Leaves of *Moringa oleifera, Ocimum gratissimum*, *Cymbopogon citratus* and *Carica papaya* , Dexamethasone, Wistar Rats, Metformin.

Accepted Date: 4 August 2017

INTRODUCTION

Diabetes mellitus is one of the whole world most common diseases caused by chronic metabolic disorder. It is mainly characterized by destruction in carbohydrates, protein, and fat metabolism caused by the complete or relative insufficiency of insulin action. It is a complex, multifactorial disease which affects the quality, quantity, and style of an individual's life (McCarty and Zimmet, 1997). It has already been established that chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and eventually the failure of organs, especially the eyes, kidney, nerves, heart and blood vessels (Sivaraj *et al.,* 2009). According to WHO report, India has 19.4 million diabetes patients (king *et al.,* 1998). When the amount of glucose in the blood increases, for example, after a meal, it triggers the release of the hormone insulin from the pancreas. Insulin stimulates muscle and fat cells to remove glucose from the blood and stimulates the liver to metabolize glucose, causing the blood sugar level to decrease to the normal level, as glucose is not metabolised; high amount of glucose is circulating

in the blood (hyperglycemia). To keep the normal level of glucose in blood, the kidney removes the extra sugar from the blood and excretes it in the urine. Because glucose is not utilized by the body cells, the body is under constant impression of hunger, and that is why diabetics feel increased appetite (polyphagia) and eat more frequently (Amos *et.al.,* 2010).

Orthodox treatment of diabetes mellitus includes modification of lifestyle, such as diet and exercise and the use of insulin or oral hypoglycemic drugs. Pharmacological agents target increased insulin secretion, decreased hepatic glucose production and increased sensitivity to insulin (Tankoyet al., 2008). Use of insulin or oral hypoglycemic agents is associated with drawbacks such as ineffectiveness on oral administration, short shelf life, requirement of constant refrigeration and in the event of excess dosage fatal hypoglycemia. The use of oral hypoglycemic drugs like sulfonylureas and biguanides is also associated with tendency to gain weight (Tankoy *et al.,* 2008). Traditional medicines (TM), are widely used in Africa, including diabetes management because of the high cost associated with orthodox medicine, inadequate health facilities and health care professionals, coupled with inadequate training of health workers (Agyareet al., 2009). There are more than 1200 plants species worldwide that are used in the treatment of diabetes mellitus and a substantial number of plants have shown effective hypoglycemic activity after laboratory testing (Eddouks *et al.,* 2005). A multitude of herbs spices and plants were observed to be effective in treatment of diabetics'worldwide (Kesari *et al.,* 2006). The medicinal plants provide a useful source of oral hypoglycemic compounds for the development of new pharmaceutical leads as well as a dietary supplement to existing therapies (Bailey and Day, 1989).

Polyherbal therapy is the use of a combination of various active ingredients'from different plants; this is a current pharmacological principle which has the advantage of producing maximum therapeutic efficacy with minimum side effects (Ebonget al., 2008). They also considered polyherbal therapy as apreferred therapeutic approach to management of diabetes mellitus because it gives a multi-factorial pathogenicity. This enhanced efficacy is believed to have been derived from medicinal plants, since they present exciting opportunities for the development of new types of therapeutics for the management of diabetes mellitus. Such phytochemicals include tea polyphenols which suppress Post-Prandial Hyperglycaemia and glucose transport across the small intestine (Yoshikawa *et al.,* 1999) and saponins which delay glucose transfer from the stomach to the small intestine (Yuan, 1998; Chatopadhya, 1998). Epicatechin has a restorative effect on pancreatic β-cells against alloxan damage (Chakravaty, 1982), and plant flavonoids which exert their antidiabetic activity via antioxidant properties (Bnouham *et al.,* 2006). These reports have accelerated the global efforts to harness and harvest those medicinal plants, which bear substantial quantity of potential phytochemicals that showed multiple beneficial effects in combating diabetes and diabetes related complications (Tiwari and Rao, 2002).

Ocimum gratissimum, Carica papaya, Cymbopogon citratus and *Moringa oleifera* are commonly found medicinal plants. *Ocimum gratissimum* is a sub-shrub and perennial plant. It belongs to the family Lamiaceae and originated from Eastern India, and spread to virtually all-tropical areas of the globe (Awah and Verla, 2010). It has been reported in several ethno-pharmacological surveys as a plant widely used in traditional medicine and readily accessible to the communities. It is known as Efinrin nla in Yoruba, Ebavbokho in Bini, Dadoya in Hausa, and Nchanwu in Igbo speaking peoples of Nigeria (Aiyeloja and Bello 2006). In Uganda, it is known as Omujaja (Tabuti *et al.,* 2003). Extensive phytochemical and pharmacological studies into the activity of the leaves of *O. gratissimum* have demonstrated its riches of both the oil and bioactive phytochemicals. Reports have shown its detoxification property in the liver and also its anti-oxidant activities (Njokuet al., 2011). The anti-inflammatory, antifungal and antibacterial properties of its essential oil have been well demonstrated (Rabelo *et al.,* 2003). Ocimum oil has been shown to calm overactive gastro-intestinal tracts in diarrhea (Orafidiya *et al.,* 2000). The inhibition of breast tumor growth and angiogenesis by the crude extract of the plant had been reported by Nangia *et al.,* 2007.

Carica papaya is the most popular and economically important species among the Caricacae family. Among the total tropical fruit production in the world, papaya was ranked third (15.4%), following production of mango (52.9%) and pineapple (26.6%) (Edward & Fredy 2012).Traditionally, different parts of the papaya plant are used in the treatment of various ailments such as asthma, ulcers, eczema, diabetes, helminth infections and fever. Research also demonstrated its beneficial traditional role in wound healing, and in the treatment of cardiovascular diseases, dengue fever, cancer, malaria, hypoglycemia, hyperlipidemia, fungal diseases and as a male contraceptive (Gupta *et al.* 1990). Central and cardiovascular effects of alcoholic extract of the leaves of Carica papaya (Yasmeen & Prabhu 2012) Papaya extracts have also been reported to have significant anti-inflammatory activity (Owoyele *et al.,* 2008; Lee *et al.*, 2011)

Cymbopogon citrate popularly known as citronella grass or lemongrass is a species which belongs to the Gramineae family, comprises approximately 500 genus and 8,000 herb species (Barbosa *et al.,* 2008). Lemongrass is a perennial grass plant widely distributed worldwide and most especially in tropical and subtropical countries (Francisco et al., 2011). When squeezed, the leaves usually produce yellow or amber colored, aromatic, essential oil (Adejuwon and Esther, 2007). Its aqueous extract is commonly used as an aromatic drink while the whole plant is well incorporated into traditional food for its lemon flavour. Traditionally, tea made from lemongrass leaves is popular among countries of South America, Asia and West Africa having been widely utilized as antiseptic, antifever, antidyspeptic, carminative and anti-inflammatory effects. Others are febrifuge, analgesic, spasmolytic, antipyretic, diuretic, tranquilizer and stomachic agent (Adejuwon and Esther, 2007; Tatiana *et al.,* 2011).

Moringa oleifera, Lam also known as *Moringa pterygosperma*, is a member of the Moringaceae family of perennial angiosperm plants, which includes 12 other species (Olson, 2002). Native of the sub-Himalayan northern parts of India, it is cultivated throughout tropical and sub-tropical areas of the world, where it is known by various vernacular names (Ramachandran *et al.,* 1980), with drumstick tree, horseradish tree, and malunggay being the most commonly found in the literature. *Moringa oleifera* is an edible plant. A wide variety of nutritional and medicinal virtues have been attributed to its roots, bark, and leaves, flowers, fruits, and seeds (Anwar *et al.,* 2007; Kumar et al., 2010). Phytochemical analyses have shown that its leaves are particularly rich in potassium, calcium, phosphorous, iron, vitamins A and D, essential amino acids, as well as such known antioxidants such as β-carotene, vitamin C, and flavonoids (Gowrishankaret al., 2010). *Moringa oleifera* have been recorded for its anti-pyretic, anti-ulcer, anti-epileptic, diuretic, cholesterol lowering, anti-diabetic (Sharma et al., 2012) and hepatoprotective activities (Huang et al., 2012).

Therefore, the present study was conducted in dexamethasone induced diabetics rats to evaluate the efficacy of combined ethanolic extract of *O. gratissimum, C. papaya, C. citratus* and *M. oleifera* at different concentrations on changes associated with diabetes.

Materials and Methods

Plant material

Fresh Leaves from the fully matured plants of *O. gratissimum, C. papaya, C. citratus and M. oleifera* were collected from different garden at Abeokuta Ogun State Nigeria, and Authenticated by a botanist at Moshood Abiola Polytechnic, Abeokuta Ogun State, Nigeria. The poly-herbal formula composed of *O.gratissimum, C. papaya, C. citratus and M. oleifera* in the same ratio (100g each).

Extraction

The leaves were cleaned separately, thinly sliced, air dried at room temperature for 21 days. Equal gram (100g) of each of the leaves were weighed and blended to give a homogeneous leaf material. Fifty grams of the mixture was extracted in 250ml of 70% ethanol by soaking the leaf mixture for 48hours with continuous shaking. The aqueous ethanol was evaporated over a water bath set at 4^0C. The extract was poured into an air tight container and stored in a refrigerator at 4^0C until used. This was then reconstituted in distilled water to give the required calculated doses equivalent to 200, 300, 400 and 500 mg/kg body weight of the rats for the experiment.

Phytochemical Screening

Each of the leaf were extracted with ethanol before combining and the extracts was subjected to qualitative analysis for phytochemical screening to test the presence of glucosides, alkaloids, flavonoids, tannins and saponins using the method of Khandelwal (2007).

Experimental animals

Thirty six female albino rats of Wistar strain of 3 months old (200–250 g) were obtained from the Department of Zoology, Animal house at Ibadan.

The animals were housed in the animal house of School Of Science and Technology, Moshood Abiola Polytechnic, Abeokuta Ogun State Nigeria, with six animals in a rat cage and maintained under controlled room temperature (32 ± 2°C) and humidity (45 ± 5%) with a 12 h D/L cycle. All the rats had free access to a normal rat pellet diet and drinking water *ad libitum*. The animals were allowed to acclimatize to the experimental environment for 1 week before the study.

Induction of diabetes: Dexamethasone and Metformin treatment

Rats of each age group were randomly divided into six experimental subgroups. Group I comprised normal control rats, receiving daily subcutaneous injections of saline for 10 days, group II-VI were Diabetes control rats and Diabetes test rats which were induced with dexamethasone (10mg/kg, i.p. in saline) for 10 days. The rats (group I-VI) were tested with glucometer every 48hours to ascertain their diabetes status. After the tenth day of treatment, the rats were weighed and their fasting blood sugar was checked with fine test strips and glucometer to determine their sugar level. Groups II-VI tested positive to diabetes with a value of 349-352mg/dL. The diabetes control group (group II) were giving metformin (100mg/kg) orally after the induction for 14 days and the diabetes test rats (group III-VI) were administered with the formulated extracts of the plants at different concentration(200-500mg/kg) orally once daily for 14 days. Blood samples were collected in the morning (between 09.00 and 10.00 h) from the tail vein of conscious rats after the 14^{th} day of treatment to determine their diabetes status and changes in animal weight were also measured within the period.

Statistical analysis

Result Data are presented as mean ± SD. The Statistical significance was evaluated by two-way analysis of variance (ANOVA). Statistical significance was accepted at the $P<0.005$ values.

Result

Phytochemical analysis of each of the leaf extract shows the presence of tannins, saponins and flavonoid as shown in Table 1. Flavonoids are also known to regenerate the damaged *β*-cells in diabetic mice (kumar*et al*., 2011; Gosh *et al*., 2009).The effects of metformin and ethanolic extracts on blood glucose levels in normal and diabetic rats after treatment of 14 days were shown in the Table 2 in which all extracts showed significant reduction ($P< 0.005$). It was observed that the extract at all the concentration show the same efficacy as standard drug metformin by lowering the blood glucose levels significantly, bringing it back to normal which is an indication of the presence of some *β*-cells, as metformin is known to stimulate insulin secretion from *β*-cells. A significant reduction in average weight was observed in dexamethasone induced diabetic rats treated with all the extracts at varying concentrations (Table 2). The decrease in weight in diabetes was due to continuous excretion of glucose and decrease in peripheral uptake of glucose and glycogen synthesis (Salau *et al*., 2003). Increase in body weight and decrease in blood glucose might be due to improving the glycemic control mechanisms and insulin secretions from remnant pancreatic cells in diabetic animals.

Table 3. Effect of mixtures at different concentration and standard metformin on body weight of dexamethasone-induced diabetic rat.

Group	B.W after induction	B.W after treatment	% increase in weight.
N.C.G	255.0±1.63	259.00±2.53	
D.C.G	167.5±0.65	174.51±0.65	4.20
D.T.G I	170.0±2.45	179.45±4.47	5.56
D.T.G II	193.3±0.14	202.33±1.06	4.67
D.T.G III	183.4±2.56	195.91±0.51	6.82
D.T.G IV	205.0±0.65	215.70±3.40	5.22

Table 1: Phytochemical Screening Result (Qualitative Analysis)

Sample	Tannins	Saponins	Flavonoids
O. gratissimum	--	++	++
C. papaya	++	++	++
C. citratus	++	++	–
M. oleifera	--	++	++

Table 2.Hyperglycemic assessment of Dexamethasone and the Extracts

2.1:Fasting blood mean analysis in mg/dL, P<0.005

Group	Normal sugar level	Blood sugar after induction	Blood sugar after treatment	% decrease in blood sugar
NCG	93.09±0.59	93.09±0.59	93.09±0.59	
DCG	106.78±2.48	349.15±0.92	82.50±0.01	76.40
DTG 1	99.48±0.74	348.24±7.44	118.44±1.75	65.99
DTG II	94.90±0.14	352.00±0.57	96.05±1.06	72.71
DTG III	92.23±1.94	352.58±2.51	112.30±1.56	68.15
DTG IV	92.53±0.39	355.73±3.92	95.68±1.59	73.10

Results expressed as mean ± SD. Treatment was done for 14 days. The data were statistically analysed by two-way ANOVA, p<0.005 were obtained which were considered significant.

Discussion

The phytochemical studies of extracts of each of the leaf plant of polyherbal combinations revealed the presence of tannins, saponins, and flavonoids as shown in table 1. Flavonoid and terpenes possess antidiabetic action (Marles and Farnsworth 1995). Effect of the flavonoids on pancreatic β-cells leading to their proliferation and secretion of more insulin have been proposed by Mahesh and Menon (2004) and Sri-Balasubashini, *et al*., (2004) as the mechanism by which they reduced hyperglycaemia caused by dexamethasone in diabetic rats. Hypoglycemic activity of the ethanolic extracts of prepared herbal mixtures and the marketed drug metformin in dexamethasone-induced diabetic rat were also evaluated. From Figure 2 it can be observed that the multi-herbal extracts have maintained the blood glucose level below 110, which is a better result. As shown in the Table, the formulated mixtures significantly reduced the blood glucose level in dexamethasone-induced diabetic rat. The hypoglycemic activity of mixture showed 66%, 73%, 68% and 73% antidiabetic activity, respectively which falls within the same range with the group treated with standard drug, metformin (76%). All the mixtures have shown potential in their role to reduce the blood glucose level.

The administration of combined leave extracts of the plants showed a potential effect which may be due to a synergy between the bioactive secondary compounds from these two plants. This agrees with another study which showed that there appears to be a complement of bioactive principles in the leaves of these plants, and this may account for their hypoglycemic action (Atangwho*et al*., 2009).

CONCLUSION

From this study we concluded that the poly herbal combination of extracts of *O. gratissimum, C. papaya, C. citratus and M. oleifera*showed synergistic activity, as the glucose levels at all the concentrations were lowered more significantly by the combination of extracts when compared to the individual extracts used alone as reported by previous researchers.

REFERENCES

Adejuwon, A.A. and Esther, O. A.(2007).Hypoglycemic and hypolipidemic effects of fresh leaf aqueous extract of *Cymbopogoncitratus* Stapf in rats. *Journal of Ethnopharmacology* 112, 440–444.

Agyare, C., Asase, A., Lechtenberg, M., Niehues, M., Deters, A.(2009). An ethnopharmacological survey and in vitro confirmation of ethnopharmacological use of medicinal plants used for wound healing in Bosomtwi-Atwima-Kwanwoma area, *Ghana.JEthnopharmacol*, 125, 393-403.

Aiyeloja, A.A., Bello, O. A.(2006). Ethnobotanical potential of Common herbs in Nigeria: A case study of Enugu State, *Edu Res and Rev*. 1(1), 16–22.

Amos, A.F., McCarty, D. J., Zimmet, P.(2010). The rising global burden of diabetes and its complications: estimates and projections to the year. *Diabetic Medicine*1997, 14 (supplement 5), S1–S85.

Anwar, F., Latif, S., Ashraf, M., Gilani, A. H.(2007).*Moringaoleifera*: a food plant with multiple medicinal uses, *Phytother. Res*. 21, 17–25

Atangwho, I. J., Ebong, P. E.,Eyong, E. U., Williams, I. O., Eteng, M. U., Egbung, G. E. (2009a). Comparative chemical composition of leaves of some antidiabetic medicinal plants: *Azadirachtaindica, Vernoniaamygdalina*and *Gongronemalatifolium. African Journal of Biotechnology*, 8(18), 4685-4689.

Bailey, L. J., Day, C.(1989). Traditional plant medicine as treatment for diabetes.*Diab. Care*, 12, 553-564.

Bnouham, M., Ziyyat, A., Melchfi, H., Yahri, A., Legssyen, A. (2006). Medicinal plants with potential antidiabetic activity– a review of 10 years of herbal medicine research (1990-2000). *International Journal of Diabetes and Metabolism*, 14, 1-25.

Chakravarthy, B.K., Gupta, S., Gode, K. D. (1982). Functional beta cell regeneration in the islets of pancreas in alloxan induced diabetic rats by (−)-epicatechin. *Life Sci*. 1:31, 2693–2697.

Chattopadhyay, R. R. (1998). Possible mechanism

of antihyperglycaemic effect of *Gymnenssylvestre*leaf extract, part I. *General Pharmacology*, 31, 495 - 496.

Ebong, P.E., Atangwho. I. J., Eyong, E. U., Egbung, G. E., 2008. The antidiabetic efficacy of combined extracts from two continental plants, *Azadirachtaindica* and *Vernoniaamygdalina*(Del).*American Journal of Biochemistry and Biotechnology*, 4(3), 239-244.

Eddouks, M., Maghrani, M., & Michel, J. B. (2005).Hypoglycemic effect of Triticumrepens P. Beauv in normal and diabetic rats. *Journal of Ethanopharmacology*, 102, 228-232.

Ghosh, D., Bera, T.K., Chatterjee, K., Ali, K. M., De, D. (2009). Antidiabetic and antioxidative effects of aqueous extract of seed of *Psoraleacorylifolia* (somraji) and seed of *Trigonellafoenum-graecum* L., (methi) in Separate and composite manner in streptozotocin-induced diabetic male Albino rat. *Tropical Journal of Pharmaceutical Research*, 1(7), 1–10.

Huang, W., Metlakunta, A., Dedousis, N., Zhang, P., Sipula, I., Dube, J.J., Scott, D.K., O'Doherty, R. M.(2010). Depletion of liver kupffer cells prevents the development of diet-induced hepatic steatosis and insulin resistance. *Diabetes*. 59, 347–357.

Kesari, A.N., Gupta, R.K., Singh, S. K., Diwakar, S., Watal G. (2006). Hypoglycemic and antihyperglycemic activity of *Aegelmarmelos*seed extract in normal and diabetic rats. *J. Ethanopharmacol*. 107, 374-379.

Khandelwal, K. R. (2007). *Practical Pharmacognosy*.18th edition. Pune, India: Nirali publication.

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

Kumar, S., Kumar, V., Prakash, O.(2010).Antidiabetic and anti-lipemic effects of *Cassia siamea* leaves extract in streptozotocin induced diabetic rats. *Asian Pacific Journal of Tropical Medicine*, 3(11), 871–873.

Kumar, S., Kumar, V., Prakash, O. (2011).Antidiabetic, hypolipidemic, and antioxidant activities of *Callistemon lanceolatus* leaves extract. *Journal of Herbs, Spices and Medicinal Plants*, 17(2), 144–153.

Mahesh, T., Menon, P. V.(2004).Quercetin alleviates oxidative stress in streptozotocin induced diabetic rats. *Phytotherapy Research* 18, 123-127.

McCarty, P., Zimmet, P. (1997). Diabetes 1994–2010 global estimate and projection.*Diabetic Care*, 20, 1785.

Nangia-Makker, P., Tait.L., Shekhar, M.P.V., Palomino, E., Hogan, V., Piechocki, M. P., Funasaka, T., Raz, A.(2007). Inhibition of breast tumor growth and angiogenesis by a Medicinal herb: *Ocimumgratissimum*, *International J. Cancer*, 121, 884–894.

Njoku, O.U., Joshua, P.E., Agu, C.V., Dim, N. C.(2011). Antioxidant properties of *Ocimumgratissimum* (Scent leaf), *New York Sci J*., 4(5), 98–103.

Orafidiya, O.O., Elujoba, A.A., Iwalewa, E.O., Okeke, I. N.(2000).Evaluation of anti-diarrhoeal properties of *Ocimumgratissimum* volatile oils and its activity against enteroaggregative Escherichia coli.*PharmacolLett*. 10, 9–12.

Phytochemicals: Present status and future prospects. *Current Science* 83, 30-37.

Rabelo, M., Souza, E.P., Soare, P.M.G., Miranda, A., Matos, J.F.A., Criddle, D. N. (2003). Anti-nociceptive properties of the essential oil of *Ocimumgratissimum* L (Labiatae) in mice, *Brazil J of Med Res*., 36, 21–524.

Ramachandran, C., Peter, K.V., Gopalakrishnan, P. K. (1980). Drumstick (*Moringaoleifera*): a multipurpose Indian vegetable, *Econ. Bot*.34, 276–283

Rates, S. M.(2001). Plant as source of drug.Toxicon, 39(5), 603-613.

Roja, G., Rao, P. S.(2000). Anti-cancer compounds from tissue cultures of medicinal plants.*Journal of Herbs, Spices and Medicinal Plants*, 7, 71-102.

Salau, B.A., Osilesi, O., Idowu, G.O., Musa, S., Ajani, E. O.(2003).Effects of fruits and vegetables on cardiovascular disease risk factors in non-insulin dependent diabetes mellitus (NIDDM) subjects, *African Journal of Medical and Pharmaceutical Sciences*, 7, 21–26.

Sharma, U., Sahu, R.K., Roy, A., Golwala, D.K. (2010). *In vivo* antidiabetic and antioxidant potential of *Stephaniahernandifolia* in streptozotocin-induced-diabetic rats.*Journal of Young Pharmacists*, 2(3), 255-260.

Sivaraj, A., Devi, K., Vinothkumar, P., Senthilkumar, B. and David, E. (2009). Anti-hyperglycemic and Anti-hyperlipidemic effect of combined plant extract of *Cassia auriculata* and *Aeglemarmelos* in streptozotocin (STZ) induced diabetic albino rats, *International Journal of Pharmtech Research,* 1:4, 1010-1016.

Sri Balasubashini, M., Rukkumani, R., Viswanathan, P., Menon, P.V. (2004).Ferulic acid alleviates lipid peroxidation in diabetic rats. *Phytotherapy Research,* 18, 310-314.

Tabuti, J.R.S., Lye, K.A., Dhillion, S. S. (2003). Traditional herbal drugs of Bulamogi, Uganda: plants, use and administration, *J Ethnopharmacol*, 88, 19–44.

Tankoy, Y., Mahdi, M., Yaro, A.H., Musa, K. Y., Mohamed, A. (2008).Hypoglycemic activity of methanolic stem bark of *Adansoniadigitata*extract on blood glucose levels of streptozocin induced diabetic Winstar rats. *International Journal of Applied Research in Natural Products,* 2, 32-36.

Tatiana, F. B. and José, M. S.(2011). Lemongrass and citral effect on cytokines production by murine macrophages, *Journal of Ethnopharmacology* 137, 909– 913

Yoshikawa, M., Schimada, H., Morikawa, T. (1997). Medicinal food stuffs vii. On the saponin constituents with glucose and alcohol absorption in inhibitory activity from a food garnish 'Tonbur' the fruit of Japanese *Kachiascoparis*(L). *Chemical and Pharmaceutical Bulletin*, 45, 1300-1305.

Yuan, Z., He, P., Ciu, J., Takeuchi, H. (1998).Hypoglycaemic effect of water soluble polysaccharide from *Auricularis auricular*-JudaeQuel.on genetically diabetic KK-AY mice. *Bioscience, Biotechnology and Biochemistry*, 62, 1898-1903.