Pharmacognosy Communications
Volume 3 | Issue 2 | Apr–Jun 2013
www.phcogcommn.org

Research Article

Hypoglycemic properties of ethanolic extracts of *Gongronema latifolium, Aloe perryi, Viscum album* and *Allium sativum* administered to alloxan-induced diabetic albino rats (*Rattus norvegicus*)

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ABSTRACT: **Background:** Plants offer a wide range of natural compounds of medicinal values to humans and domestic animals. **Objective:** The ethanolic extracts of *Gongronema latifolium*, *Aloe perryi, Viscum album* (leaves) and *Allium sativum* (bulb) were investigated for their phytochemical/biochemical constituents and hypoglycemic properties. **Materials and Methods:** Hypoglycemia was induced in rats by a single dose (140 mg/kg) of intra-peritoneal injection of alloxan monohydrate in citrate buffer (pH 4.5). Suspensions of the ethanolic extracts were administered by intra-peritoneal injection at doses of 2 mg/kg every 16 h for 54 h. Collection of blood samples for estimation of fasting blood glucose (FBG) was carried out at regular time intervals of 0, 16, 32, 48 and 54 h, using the glucose oxidase method. **Results:** Phytochemical and biochemical screening showed the presence of saponins, tannins, flavonoids, proteins and carbohydrates in the four plant tissues under investigation. *A. sativum* and *G. latifolium* also tested positive for the presence of alkaloids. The capacities of the four ethanolic extracts to reduce FBG concentrations in treated rats at the 54 h were in the order: *A. perryi* > *G. latifolium* > *A. sativum* > *V. album*. Comparatively, at t = 16 h, FBG concentration of *V. album* treated rats was not significantly different ($p > 0.05$) from those of *G. latifolium* treated group. Likewise, FBG concentration of rats treated with *V. album* extract did not show a significant difference ($p > 0.05$) compared to the group administered with extract of *A. sativum*. **Conclusion:** The four plant extracts used in the present study exhibited approximately the same capacity to act as hypoglycemic agents in the treated rats and correlate with the therapeutic capacity of the standard drug, glimepiride.

KEYWORDS: Hypoglycemia, phytochemical, *A. perryi, G. latifolium, A. sativum, V. album*, glimepiride

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia and glycosuria produced by an absolute or relative insulin insufficiency (Insulin-Dependent Diabetes Mellitus (IDDM)) or insulin resistance by peripheral cells (Non-Insulin-Dependent Diabetes Mellitus (NIDDM)), or both.[1] The disease presents other metabolic and anatomic distortions and disturbances, including retinopathy, neuropathy, nephropathy, hyperlipidemia, hypercholesterolemia, ketosis, atherosclerotic coronary artery and peripheral atherosclerotic vascular diseases.[2,3] The individual also experiences weight loss, pathologic changes in the eye, renal dysfunction and neuropathy.[4,5] Oxidant-free radicals have been implicated in the pathogenesis of IDDM.[1,6,7] In experimental animals, injection and subsequent metabolism of 2, 4, 5, 6-tetraoxypyrimidine (alloxan) induces specific DNA fragmentation in pancreatic islets and cell damage has been attributed to the production of toxic free radicals.[1,8] Alloxan-treated animals are widely used as models for IDDM studies.[1,3,9–13] The reason for the high sensitivity of β-cells to alloxan is not clear, although there are speculations on the connection between alloxan sensitivity and the incidence of IDDM.

Plants offer a wide range of natural compounds of medicinal values to humans and domestic animals. *Gongronema*

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DOI: 10.5530/pc.2013.2.4

latifolium (commonly called 'arokeke' and 'utazi' in the South Western and South Eastern parts of Nigeria) is a tropical rainforest plant primarily used as a spice and vegetable in traditional folk medicine.[2,14] *G. latifolium* has anti-plasmodial activity;[15] this supports the traditional use of the leaf extract of the plant for local treatment of malaria. Reports have shown that *G. latifolium* has anti-sickling activities and is effective in the treatment of sore gums, colic, dyspepsia and anti-helminthic.[16] *Aloe perryi* belongs to the family of *Liliaceae*, and the use of *A. vera* for the alleviation of constipation has been documented in Wistar rats.[17] There are no reports on the use of *A. perryi* in ameliorating DM in human. Another member of the *Liliaceae* family, *Allium sativa* (garlic), apart from its medicinal purposes, is also used as seasoning in Africa, Southern Europe and Asia. It is a natural source of selenium to the body for proper immune response, and acts as an antioxidant.[18] Extracts from *Viscum album* (Mistletoe) are widely used as alternative cancer and cardiovascular disease therapies in Europe and have been recognised to induce apoptosis.[19–22] The hypoglycemic and antioxidant activity of *V. album* extract has also been investigated.[21]

Although a variety of drugs are available for the treatment and management of DM, herbal preparations are still prescribed widely as alternatives to synthetic ones (even when their biologically active compounds are unknown) because of their minimum side-effects and relatively low cost. Furthermore, for many centuries plants have been used medicinally for the treatment of diverse disorders/ailments and there are numerous documented claims of herbal remedies for DM. Almost five decades ago, Jain *et al.*,[23] posited that ingestion of *Allium cepa* (onion) and *A. sativum* (garlic) juice resulted in better utilization of glucose in rabbits. Recently, the applications of natural substances for the prevention, management and treatment of DM have been reported by several researchers and there are increasing search for herbal hypoglycemic agents.[12,13,24,25] In view of this, it has been considered pertinent to investigate the hypoglycemic properties of various extracts of *G. latifolium, A. perryi, V. album* and *A. sativum* in alloxan induced diabetic *Rattus norvegicus*.

MATERIALS AND METHODS

Collection of plant specimens

Fresh samples of *G. latifolium, A. perryi, V. album* and *A. sativum* were harvested between October and November, 2011 from the Botanical Gardens of Imo State University and Federal University of Technology, Owerri, Nigeria. The plant specimens were identified and authenticated by Dr. F. N. Mbagwu at the Herbarium of the Department of Plant Science and Biotechnology, Imo State University, Owerri. A voucher specimen was deposited at the Herbarium for reference purposes.

Preparation of extracts

Plant samples were washed under a continuous stream of of distilled water for 15 min and air-dried at room temperature for 5 h. The separate leaves were further dried for 5 h in an oven at 60°C and subsequently ground with a ceramic mortar and pestle. Twenty-five grams (25 g) of each pulverized specimen was suspended in 250 mL of ethanol/water mixture (1:2 *v/v*) in stoppered flasks and allowed to stand for 24 h. The suspensions were filtered with Whatman No. 24 filter papers. The filtrates were concentrated in a rotary evaporator at 50°C and dried in vacuum desiccators. The yield was calculated to be *G. latifolium* (3.4% *w/w*), *A. perryi* (3.1% *w/w*), *V. album* (2.2% *w/w*) and *A. sativum* (3.5% *w/w*). These extracts were finally suspended in phosphate buffered saline (PBS) solution (extract vehicle), osmotically equivalent to 100 g/l PBS (90.0 g NaCI, 17.0 $Na_2HPO_4.2H_2O$ and 2.43 g $NaH_2PO_4.2H_2O$), and used in all the studies with doses expressed in milligram per kilogram body weight (mg/kg) of the animals.

Phytochemical and biochemical study

Phytochemical and biochemical screening was carried out for the presence of tannins, carbohydrates, flavonoids, saponin, alkaloids, glycosides and proteins as described by Ayoola *et al.*[26]

Experimental animals

Wistar albino rats (8–10 weeks of age) of both genders and weighing 17–21 g of were obtained from an animal house at the University of Port Harcourt, Port Harcourt, Nigeria. Throughout the study, rats were fed with standard commercial feed (Ewu Feed Mills, Edo State, Nigeria) and water *ad libitum*, in well-ventilated stainless steel cages. After randomization on a weight basis, the rats were acclimatized for a period of 7 days at ambient temperatures of 25 ± 5°C, 30–55% of relative humidity and 12 h light/12 h darkness cycle. The handling of the animals was in accordance with the standard principles of laboratory animal care of the United States National Institutes of Health (NIH, 1978).

Induction of diabetes

Diabetes was induced in the rats as previously described by Mohini *et al.*[27] A single dose (140 mg/kg) of alloxan monohydrate in citrate buffer (pH 4.5) was administered to the rats via intra-peritoneal injection. Hyperglycemia was confirmed 48 h after alloxan injection.[28] Surviving

rats with FBG concentrations higher than 250 mg/dL were included in the study.[29,30]

Study design and fasting blood glucose estimation

Experimental animals were deprived of food and water for 16 h before the commencement of the feeding experiment. A total of twenty-eight (28) rats were divided into seven groups (n = 4) each as follows:

- Group Control-Normal (Control-N): The animals of this group were non-diabetic and received only PBS (1 ml/kg/16 h, i. p.) for 54 h.
- Group Control-Diabetic (Control-D): The animals of this group were diabetic and received PBS (1 ml/kg/16 h, i. p.) for 54 h.
- Group T1 (D + *V. album*): The animals of this group were diabetic and received *V. album* (2 mg/kg/16 h, i. p.) for 54 h.
- Group T2 (D + *A. sativum*): The animals of this group were diabetic and received *A. sativum* (2 mg/kg/16 h, i. p.) for 54 h.
- Group T3 (D + *G. latifolium*): The animals of this group were diabetic and received *G. latifolium* (2 mg/kg/16 h, i. p.) for 54 h.
- Group T4 (D + *A. perryi*): The animals of this group were diabetic and received *A. perryi* (2 mg/kg/16 h, i. p.) for 54 h.
- Group T5 (D + Glimepiride): The animals of this group were diabetic and received Glimepiride (0.09 mg/kg/16 h, i. p.) for 54 h.

Blood samples were drawn from the tip of the tails of the rats at regular time intervals of 0, 16, 32, 48 and 54 h for FBG estimation. FBG was estimated by glucose oxidase method according to the Randox® kit manufacturer's procedure (Randox® Laboratories Ltd. Ardmore, United Kingdom).

Statistical analysis

The results were expressed as mean ± SEM, and statistically analyzed by one way ANOVA followed by Dunnett test, with level of significance set at $p < 0.05$.

RESULTS

Phytochemical and chemical screenings showed the presence of tannins, saponins, flavonoids, proteins and carbohydrates in the four plant tissues under investigation. *A. sativum* and *G. latifolium* tested positive for the presence of alkaloids.

The FBG concentrations (mg/dl) of the seven (7) groups of rats within the experimental time (t) = 54 h are presented in Figure 1. The FBG concentrations of the Control-N and Control-D groups showed low variability. The FBG concentration of Control-N group ranged between 96.5 ± 0.54 and 97.5 ± 0.71 mg/dl ($54 \geq t \geq 0$; $p > 0.05$), whereas Control-D group was between 232.5 ± 1.26 and 233.5 ± 1.43 mg/dl ($54 \geq t \geq 0$; $p > 0.05$). As an overview of the results, all the treated rats (Groups T1-T5) exhibited reductions in FBG concentrations as the experimental time progressed, while the Group Control-D showed little change. Comparatively, the standard drug (Glimepiride) exhibited the highest capacity to reduce FBG concentrations in treated rats (Group T5: D + Glimepiride).

The capacities of the four ethanolic extracts to reduce FBG concentrations in treated rats by 54 h of the experiment were in the order: *A. perryi* > *G. latifolium* > *A. sativum* > *V. album* (Table 1). Indeed, the *A. perryi* extract caused the reduction of FBG concentration from 240 ± 1.11 mg/dl ($t = 0$ h) to 189 ± 1.02 mg/dl at $t = 54$ h, representing 22.50% reduction in FBG concentration. The administration of *V. album* extract to rats caused a FBG reduction of 15.55 ± 0.92% at $t = 54$ h (Table 1). The FBG concentrations of the *V. album, A. sativum* and *A. perryi* treated groups, as well as for the standard control group (D + Glimepiride) showed significant differences ($p < 0.005$) between each preceding time intervals of treatment when $t > 16$ h. In contrast, *G. latifolium* extracts induced no significant ($p > 0.005$) reduction in FBG concentration between the 32 and 48 h. Generally, within the experimental time range ($54 \geq t \geq 0$) h, the four extracts caused a progressive reduction in FBG concentrations but did not exhibit the capacity to return FBG concentrations to the normal levels observed in Control N animals (96.8 ± 0.57 mg/dl) in the rats during the experimental period.

At $t = 16$ h, the FBG concentration in D + *V. album* rats was not significantly different ($p > 0.05$) from those of the D + *G. latifolium* group. Likewise, the FBG concentration

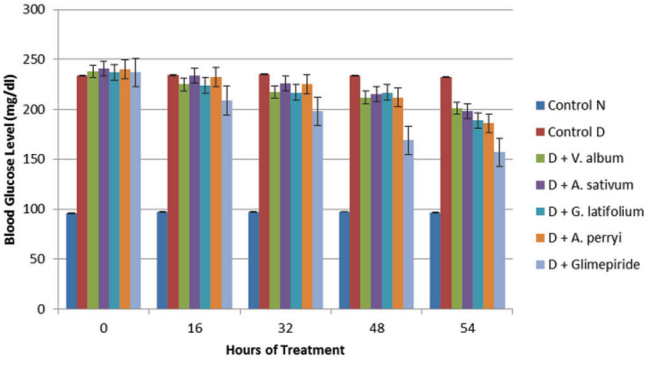

Figure 1. Comparative effect of ethanolic extracts of *V. album, A. sativum, G. latifolium A. perryi* and Glimepiride on FBG in alloxan-induced diabetic rats.
Percentages of FBG concentration are mean of n ± SEM of four (4) blood samples.

Table 1: Reduction in levels FBG concentrations in the presence of ethanolic extracts of *V. album*, *A. sativum*, *G. latifolium* *A. perryi* and glimepiride in alloxan-induced diabetic rats

	Percentage (%) Reduction in FBG Concentration				
Time (h)	**D + *V. album***	**D + *A. sativum***	**D + *G. latifolium***	**D + *A. perryi***	**Glimepiride**
16	5.46 ± 1.08	2.87 ± 1.23	5.49 ± 1.20	3.33 ± 1.09	11.81 ± 0.88
32	8.61 ± 0.99	6.03 ± 0.96	8.44 ± 0.89	6.25 ± 0.95	16.46 ± 1.11
48	10.93 ± 0.89	10.60 ± 1.00	8.44 ± 0.99	11.67 ± 1.07	28.69 ± 0.89
54	15.55 ± 0.92	17.67 ± 0.78	20.25 ± 0.92	22.50 ± 1.02	33.76 ± 0.99

Percentage reductions in the values of FBG concentration are mean of n ± SEM of four (4) blood samples.

of rats treated with extract *V. album* did not show a significant difference ($p > 0.05$) compared to the group administered with extract of *A. sativum* (Table 1).

DISCUSSION

The results of the present study supports previous reports on the hypoglycemic properties of *Viscum album* leaf extracts,[21,31] *Eugenia floccosa* Bedd leaf extracts,[32] *Rubus ellipticus* fruit extracts,[13] matured fruits extracts of *Diospyros peregrina,*[3] *Vinca rosea* whole plant extracts,[24] *Terminalia catappa* Linn fruit extracts[33] and onion and garlic extracts.[34] A target-based therapeutic approach towards diabetes mellitus treatment using medicinal plants has been extensively discussed.[35] These previous studies suggest that the active principles of these plant extracts exerted therapeutic benefits by either mimicking the physiologic actions of insulin and/or facilitating insulin secretion.

An earlier report[31] stated that *V. album* contains water-soluble and heat-resistant natural product(s) that enhance the release of insulin in hyperglycemic streptozotocin-induced diabetic rats. Although their report could not establish whether the β-amyrin, tyramin, quercitin, syringin and flavoyedorinin A and B components of the leaf extract was responsible for its hypoglycemic property, they noted that the hypoglycemic action of *V. album* extract was not mediated by lectins. In the present study, phytochemical screening of *V. album* extract showed the presence of flavonoids. Flavonoids are potent hypoglycemic agents.[36–38] Therefore, the presence of flavonoids in the *V. album* extract was responsible for its hypoglycemic activity, possibly by the stimulation of insulin secretion.[31] In another study, flavonoids were found to possess antioxidant activity as shown by promoting increased activity of superoxide dismutase (SOD) and decreased plasma malondialdehyde (MDA) concentrations in diabetic rats.[37] Thus, the presence of flavonoids may also act to antagonize the generation of free radicals by alloxan and the associated pathophysiology of the diabetic state.

The hypoglycemic property of *A. sativum* extract reported here are in accordance with previous reports.[39,40] Ayodhya *et al.*[39] states that the hypoglycemic activity of the ether extract of *A. sativum* was due to increased insulin-like activity, while Chauha *et al.*[41] suggested that oral administration of ethanolic extract of *A. sativum,* facilitated by its Allicin content, acted by stimulating insulin secretion from pancreatic β cells. The phytochemical contents of the ethanolic extract of *A. sativum* in our study revealed the presence of varieties of plant natural agents found to possess hypoglycemic properties. Worthy of note are the tannins,[33,42,43] flavonoids[36–38,43] and alkaloids.[44] β-carotene, which was not did not assayed in the current study, has also been reported to have hypoglycemic effects.[33]

Ugochukwu and Babady,[45] showed that ethanolic extracts from *G. latifolium* leaves contained hypoglycemic potency, which was thought to be mediated through the activation of hexokinase, phosphofructokinase, glucose-6-phosphate dehydrogenase and inhibition of glucokinase enzymatic activity in the livers of diabetic rats. Another report[46] shows that ethanolic extracts of *G. latifolium* appeared to be more effective in reducing oxidative stress, lipid peroxidation and increased reduced glutathione/oxidized glutathione (GSH/GSSG) ratio, thus confirming the ethnopharmacological use of *G. latifolium* in ameliorating the oxidative stress associated with diabetics. Rajasekaran *et al.*[47] reported the presence of several hypoglycemic-activity-possessing elements in the gel of *A. perryi*. They also showed that streptozotocin-induced diabetic rats treated with the ash of *A. perryi* resulted in hypoglycemic action. Thus, the presence of various inorganic trace elements in the gel appeared to account for the hypoglycemic nature of the plant.

In summary, the four plant extracts used in the present study exhibited approximately the same hypoglycemic capacity in the treated rats. There was also an extent of correlation with the therapeutic capacity of the standard drug, glimepiride.

REFERENCES

1. Gwarzo MY, Nwachuku VA, Lateef AO. Prevention of alloxan induced diabetes mellitus in rats by vitamin a dietary supplementation. Asian Journal of Animal Sciences. 2010; 4:190–6.
2. Ugochukwu NH, Babady NE, Cobourne M, Gasset SR. The effect of *Gongronema latifolium* extracts on serum lipid profile and oxidative stress in hepatocytes of diabetic rats. Journal of Bioscience. 2003; 28:1–5.
3. Dewanjee S, Bose SK, Sahu R, Mandal SC. Antidiabetic effect of matured fruits of *Diospyros peregrina* in alloxan induced diabetic rats. International Journal of Green Pharmacy. 2008; 95–9.
4. Ene AC, Nwankwo EA, Samdi LM. Alloxan-induced diabetes in rats and the effects of black caraway (*Carum carvi* l.) oil on their body weight. Research Journal of Medicine and Medical Sciences. 2007; 2(2):48–52.
5. Andrew IR, Scott BE, Clarke HH, Michael DE, Scott CB. Microvascular complications in cystic fibrosis-related diabetes mellitus. a case report. Journal of the Pancreas. 2000; 14:208–10.
6. Baynes JW, Thorpe SR. Role of oxidative stress in diabetic complications. Diabetes. 1999; 48:1–9.
7. El-Missiry MA, El Gindy AM. Amelioration of alloxan induced diabetes mellitus and oxidative stress in rats by oil of *Eruca sativa* seeds. Annals of Nutrition and Metabolism. 2000; 44:97–100.
8. Lankin VZ, Korchin VI, Konovalova GG, Lisina MO, Tikhaze AK, Akmaev IG. Role of antioxidant enzymes and antioxidant compound probucol in antiradical protection of pancreatic beta-cells during alloxan-induced diabetes. Bulletin of Experimental Biology and Medicine. 2004; 137:20–3.
9. Dhandapani S, Subramanian RV, Rajagopal S, Namasivajam N. Hypolipidemic effect of *Cuminum cyminum* L. on alloxan-induced diabetic rats. Pharmaceutical Research. 2002; 46:3.
10. Visser J, Groen H, Klatter F, Rozing J. Timing of pentoxifylline treatment determines its protective effect on diabetes development in the Bio Breeding rat. European Journal of Pharmacy. 2002; 445:133.
11. Gül N, Cebesoy S, Özsoy N. Lectins binding during alloxan-induced diabetes in rat soleus muscle. African Journal of Biotechnology. 2008; 7(8):926–30.
12. Rotimi SO, Omotosho OE, Rotimi OA. Persistence of acidosis in alloxan-induced diabetic rats treated with the juice of *Asystasia gangetica* leaves. Pharmacognosy Magazine. 2011; 7(25):25–30.
13. Sharma US, Kumar A. Anti-diabetic effect of *Rubus ellipticus* fruits extracts in alloxan-induced diabetic rats. Journal of Diabetology. 2011; 2:4.
14. Eleyinmi AF. Chemical composition and antibacterial activity of *Gongronema latifolium*. Journal of Zhejiang University Science. 2007; 8(5):352–8.
15. Akuodor GC, Idris-Usman M, Anyalewechi N, Odo E, Ugwu CT. et al., *In vivo* antimalarial activity of ethanolic leaf extract of *Verbena hastata* against *Plasmodium berghei* in mice. Journal of Herbal Medicine and Toxicology. 2010; 4(2):17–23.
16. Egunyomi A, Moody JO, Eletu O. M. Antisickling activities of two ethnomedicinal plant recipes used for the management of sickle cell anemia in Ibadan, Nigeria. African Journal of Biotechnology. 2009; 8(1):020–5.
17. Ashafa AOT, Sunmonu TO, Abass AA, Ogbe AA. Laxative potential of the ethanolic leaf extract of *Aloe vera* (L.) Burm. f. in Wistar rats with loperamide-induced constipation. Journal of Natural Pharmaceuticals. 2011; 2:158–62.
18. http.//www.complete-herbal.com/details/garlic.htm. Retrieved, 23 April, 2012.
19. Büssing A, Schietzel M. Apoptosis-inducing properties of *Viscum album* L. extracts from different host trees correlate with their content of toxic mistletoe lectins. *Anticancer Research*. 1999; 19(1A):23–8.
20. Hajto T, Hostanska K, Berki T, Palinkas L, Boldizsar F, Nemeth P. Oncopharmacological perspectives of a plant lectin (*Viscum album* Agglutinin-I). Overview of recent results from *in vitro* experiments and *in vivo* animal models, and their possible relevance for clinical applications. Evid Based Complement Alternative Medicine. 2005; 2(1):59–67.
21. Shahaboddin ME, Pouramir M, Moghadamnia A, Lakzaei M, Mirhashemi SM, Motallebi, M. Anti-hyperglycemic and antioxidant activity of *Viscum album* extract. African Journal of Pharmacy and Pharmacology. 2011; 5(3):432–6.
22. European Medicines Agency. Assessment report on *Viscum album* L., herba. *www.ema.europa.eu.* 2011; Retrieved on 23rd April, 2012.
23. Jain RC, Vyas CR. Garlic in alloxan-induced diabetic rabbits. American Journal of Clinical Nutrition. 1975; 28:684–5.
24. Ahmed MF, Kazim SM, Ghori SS, Mehjaheen SS, Ahmed SR. et al. Antidiabetic activity of *Vinca rosea* extracts in alloxan-induced diabetic rats. International Journal of Endocrinology. 2010 (2010),
25. Mungle AN, Bodhankar NM, Chandak KK. Anti-diabetic potential of *Dolichandrone falcata* leaves in alloxan induced diabetic rats. International Journal of Research in Pharmaceutical and Biomedical Sciences. 2012; 3(1):319–24.
26. Ayoola GA, Folawewo AD, Adesegun SA, Abioro OO, Adepoju-Bello AA, Coker HAB. Phytochemical and antioxidant screening of some plants of apocynaceae from South West Nigeria. African Journal of Plant Science. 2008; 2(9):124–8.
27. Mohini P, Subhash P, Manohar P, Abhijit T, Vijay N. Effect of thespesone-vanadium complex in alloxan induced diabetic rats. African Journal of Pharmacy and Pharmacology. 2012; 6(10):692–7.
28. Mandal SC, Mukharjee PK, Saha K, Das J, Pal M, Saha BP. Hypoglycemic activity of *Ficus racemosa* L. (Moraceae) leaves in streptozotocin induced diabetic rats. Journal of Natural Products. 1997; 3:38–41.
29. Ghosh S, Suryawanshi SA. Effect of *Vinca rosea* extracts in treatment of alloxan diabetes in male albino rats. Indian Journal of Experimental Biology. 2001; 39:748–59.
30. Murali B, Upadhyaya UM, Goyal RK. Effect of chronic treatment with *Enicostemma littorale* in non-insulin dependent diabetic (NIDDM) rats. Journal of Ethnopharmacology. 2002; 81:199–204.
31. Gray AM, Flatt PM. Insulin-releasing and insulin-like activity of the traditional anti-diabetic plant *Coriandrum sativum* (coriander). British Journal of Nutrition. 1999; 81:203–9.
32. Kala SMJ, Tresina PS, Mohan VR. Antioxidant, anti-hyperlipidaemic and anti-diabetic activity of *Eugenia floccosa* Bedd leaves in alloxan induced diabetic rats. Journal of Basic and Clinical Pharmacy. 2012; 3(001):235–40.
33. Nagappa AN, Thakurdesai PA, Venkat Rao N, Singh J. Antidiabetic activity of *Terminalia catappa* Linn fruits. Journal of Ethnopharmacology. 2003; 88:45–50.
34. El-Demerdash FM, Yousef MI, Abou El-Naga NI. Biochemical study on the hypoglycemic effects of onion and garlic in alloxan-induced diabetic rats. Food and Chemical Toxicology. 2006; 43:57–63.
35. Prabhakar PK, Doble M. A target based therapeutic approach towards diabetes mellitus using medicinal plants. Current Diabetes Reviews. 2008; 4:291–308.
36. Zhu Y, Zhang Y, Liu Y, Chu H, Duan H. Synthesis and biological activity of trans-tiliroside derivatives as potent anti-diabetic agents. Molecules. 2010; 15:9174–83.
37. Cho BO, Ryu HW, Jin CH, Choi DS, Kang SY, et al. Blackberry extract attenuates oxidative stress through up-regulation of Nrf2-dependent antioxidant enzymes in carbon tetrachloride-treated rats. Journal of Agricultural and Food Chemistry. 2011; 59(21):11442–8.
38. Najafian M, Ebrahim-Habibi A, Yaghmaei P, Parivar K, Larijani B. Core structure of flavonoids precursor as an anti-hyperglycemic and anti-hyperlipidemic agent. An *in vivo* study in rats. Acta Biochimica Polonica. 2010; 57(4):553–60.
39. Ayodhya S, Kusum S, Anjali S. Hypoglycemic activity of different extracts of various herbal plants Singh International Journal of Research in Ayurveda and Pharmacy. 2010; 1(1):212–14.
40. Patel DK, Prasad SK, Kumar R, Hemalatha S. An overview on anti-diabetic medicinal plants having insulin mimetic property. Asian Pacific Journal of Tropical Biomedicine. 2012; (2012):320–30.
41. Chauhan A, Sharma PK, Srivastava P, Kumar N, Duehe R. Plants having potential anti-diabetic activity. a review. Der Pharmacia Lettre. 2010; 2(3):369–87.
42. Teotia S, Singh M. Hypoglycemic effect of *Prunus amygdalusseeds* in albino rabbits. Indian Journal of Experimental Biology. 1997; 35:295–6.
43. Ali RB, Atangwho IJ, Kuar N, Mohamed EAH, Mohamed AJ et al., Hypoglycemic and anti-hyperglycemic study of *Phaleria macrocarpa* fruits pericarp. Journal of Medicinal Plants Research. 2012; 6(10):1982–90.
44. Badole S, Patel N, Bodhankar S, Jain B, Hardwar S. Anti-hyperglycemic activity of aqueous extract of leaves of *Cocculus hirsutus* (L.) Diels in alloxan-induced diabetic mice. Indian Journal Pharmacology. 2006; 38:49–53.
45. Ugochukwu NH, Babady NE. Antihyperglycaemic of effect aqueous and ethanolic extracts of *Gongronema latifolium* leaves on glucose and glycogen metabolism in livers of normal and streptozotocin induced diabetic rats. Life Science. 2003; 73(150):1925–38.
46. Ngozi H, Ugochukwu HN, Makini K, Cobourne MK. Modification of renal oxidative stress and lipid peroxidation in streptozotocin-induced diabetic rats treated with extracts from *Gongronema latifolium* leaves. Clinica Chimica Acta. 2003; (336):1–2.
47. Rajasekaran S, Sivagnanam K, Subramania S. Mineral contents of *Aloe vera* leaf gel and their role on streptozotocin-induced diabetic rats. Biological Trace Element Research. 2005; 108(1–3):185–96.