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ORIGINAL RESEARCH ARTICLE

Hypoglycemic and Hypolipidemic Effects of *Mimusops elengi* Linn Extracts on Normoglycaemic and Alloxan-Induced Diabetic Rats

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ABSTRACT

To evaluate the hypoglycemic effect of methanolic extracts of flower and leaves of *Mimusops elengi* Linn (*Sapotaceae*) in normoglycaemic and alloxan-induced diabetic rats. Both extracts of *Mimusops elengi* Linn were administered orally (100 mg/kg, body weight) to normal and alloxan-induced diabetic rats. The fasting blood glucose (FBG), oral glucose tolerance test (OGTT) and alloxan-induced diabetic models were performed for the hypoglycemic effects and compared with tolbutamide (100 mg/kg, body weight), a standard drug. Both the extracts (MFE and MLE) showed marked decreased ($P < 0.01$) in blood glucose level in normotensive rats within 2 h after oral administration. A significant ($P < 0.001$) decreased in elevated blood glucose level was observed in glucose loaded animals. The onset of action of action in glucose tolerance test (OGTT) was 30 min. MFE and MLE significantly ($P < 0.01$) decreased blood glucose level from 221.83±3.73, 210.50±2.51 to 157.00±9.89, 173.33±11.21 mg/dl respectively after 7 days treatment in alloxan-induced diabetic rats. MFE and Tolbutamide in treated animals showed significant ($P < 0.001$) improvement of body weight up to 5.24 %, 3.35% respectively. In diabetic rats, MFE and MLE treatment at a dose of 100 mg/kg, body weight for 7 days significantly ($P < 0.01$) decreased triglycerides levels compared to the diabetic control group. The present study demonstrated the potential hypoglycemic and hypolipidemic effects of flower and leaves of *Mimusops elengi* Linn and support the traditional use of the plant as hypoglycemic and hypolipidemic agents.

Keywords: *Mimusops elengi* Linn, hypoglycemic activity, alloxan-induced diabetes, blood glucose level.

INTRODUCTION

Diabetes mellitus is a group of disorders characterized by hyperglycemia and defective metabolism of glucose and lipid [1]. These metabolic disorders have a significant impact on the quality of life, health and life expectancy of patients [2]. The characteristic symptoms of diabetes are polyuria, polydipsia, polyphagia, pruritus and unexpected weight loss, etc. Over a period of time diabetes develops complications such as nephropathy, retinopathy and neuropathy [3]. Impaired glucose tolerance and the metabolic disorder often lead to development of type II diabetes. A number of important epidemiological studies revealed the relationship between hyperglycemia and an increased risk of cardiovascular disease [4].

It is the most widespread disease in the world, disturbing 25% of population and badly affect 150 million people and is set to increase up to 300 million by 2025 [5]. The conventional drugs used for diabetes mellitus such as sulfonylureas, biguanides, α- glucosidase inhibitors, glinides, are associated with several side effects [6]. Ethanopharmacological survey indicates that more than 1200 plants are used throughout the world for their hypoglycemic property. The plants extracts that are used for antidiabetic activity may contain one or more compound to decrease blood sugar level suggesting that the natural constituents could act separately or synergistically to produce hypoglycemic effect [7]. Traditional antidiabetic plants and plant extracts which are being used for the treatment of diabetes are considered as a source for new oral hypoglycemic compounds, that are not only effective in the management of diabetes but also having minimal or less side effects [8].

Mimusops elengi Linn belongs to the family Sapotaceae [9]. The family comprises mostly of large evergreen trees, less commonly shrubs. It

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grows wild in Sothern India, Burma and Pakistan. Commonly known as Indian Medlar Tree, Bullet Wood, Spanish cherry (English), Molsari (Urdu), Bakul, Bolsari (Hindi), Pogada (Telugu).

Various morphological parts of the plant are used as a remedy in various ailments in the indigenous system of medicine for centuries. The extract of the flower is salutary not only in heart diseases but also used as anti diuretic agent in polyuria condition. It alleviates the toxins, hence used as an anti-toxin [10]. Floral part of the plant produce copious discharge from nose, sniffing is employed to relieve headache [11]. It is also used to prepare lotion for wounds and ulcers; dried powder is a brain tonic and is useful to relieve cephalagia. Internally bark skin is benevolent in leucorrhoea, menorrhagia and is also known to have antiulcer activity [12, 13]. Bark is used as a tonic, febrifuge, as a gargle for odontopathy, inflammation and bleeding of gums. Unripe fruit is used as a masticatory and will help to fix loose teeth [14]. Seed bark decoction is used as aphrodisiac, cardio tonic and to treat mouth ulcer. Latex is applied to treat scabies and skin sores [15]. Leaves are used as an antidote in snakebite [16].

The presence of saponins, alkaloid, steroids and terpenoids has previously been reported form *M. elengi* [17]. Flower contains volatile oil [18], D-mannitol, beta-sitosterol and beta-sitosterol-D-glycoside [19]; leaves contain sterols, reducing sugar, tannins; stem bark contain tannins, spinosterol and taraxerol [20].

Mimusops elengi Linn is reported to possess antihyperglycemic activity. Bark of this plant exhibited potential to treat diabetes [21-23]. Aqueous, alcoholic and ethanolic extracts of leaves of *M. elengi* showed antidiabetic results [24, 25]. Powder of the leaves mixed in milk is administered twice a day for diabetes [26]. Considering the traditional claim of the plant as an anti diabetic agent, the present study was aim to evaluate hypoglycemic and hypolipidemic properties of methanolic extracts of flower and leaf of *Mimusops elengi* Linn.

MATERIALS AND METHODS

Plant material

The flowers and leaf of *Mimusops elengi* Linn were collected from the premises of University of Karachi, Pakistan, in the month of July 2009. The plant materials were identified and authenticated by Prof. Dr. Ghazala H. Rizwani, Faculty of Pharmacy, University of Karachi, Pakistan. A voucher specimen (083) was deposited at the herbarium of the Department of Pharmacognosy, Faculty of Pharmacy, University of Karachi, Pakistan.

Preparation of extracts

After the collection of flower and leaves, both plant parts were dried separately under shade. 500 g of flower and leaf were soaked in methanol (5L) at room temperature separately for seven to ten days. After that methanol was filter through Whatmann filter paper No. 1 and the extract was concentrated under reduced pressure and controlled temperature on a rotary evaporator (Buchi, Switzerland). The yield of flower extract (MFE) and leaf extract (MLE) were 27.2 g (5.44%) and 60 g (12.0%) respectively.

Experimental animals

Albino rats weighing 130-200 g and Swiss albino mice 20-25 g was used for the experiments. All animals were housed in standard cages at a temperature of 27± 2°C. They were exposed to the alternate cycle of 12 h of darkness and light and fed with standard laboratory diet (PCSIR Laboratories, Karachi, Pakistan) and water. The animals were fasted for at least 12 h before each experiment, but free access to water was available.

Chemicals

Absolute Methanol (Merck, Germany), Tolbutamide (Merck, Germany), Glucose (Merck, Germany), Alloxan monohydrate (Sigma Chemical, USA).

Experimental protocol

Acute Toxicity studies

The mice (20-25 g) were divided into control and test groups containing six mice in each group. Normal saline was administered to the control group while the test groups were administered with graded doses of the extracts (500 mg/kg - 5000 mg/kg, body weight) respectively. The parameters that were observed including hyperactivity, sense of pain and touch, convulsion, phonation, aggression, increased or decreased respiration, laccrimation, social interaction, urination and defecation. All animals were observed for mortality for one week [27].

Determination of Blood Glucose Levels

Fasting blood glucose level was determined using a Glucometer-elite Commercial Test Strips (Bayer, USA) based on glucose oxidase method. Blood sample were collected from the tip of tail at the defined times in the protocol.

Evaluation of Hypoglycemic activity of the extracts

The hypoglycemic activity of the plant extracts was evaluated by fasting blood glucose in normal rats and oral glucose tolerance test [28]. The anti-

diabetic potential of the extracts were tested using alloxan-induced diabetic rats [29] with slight modification.

Fasting blood glucose (FBG) in normal rats

Rats were divided into 3 groups of six animals. Group I served as control and administered normal saline through oral intubation. Other two groups were orally administered with 100 mg/kg body weight MFE and MLE respectively. Blood samples were collected from tip of tail just prior to 1, 2, and 3 h. Blood glucose level were determine by Glucometer.

Oral glucose tolerance test (OGTT)

Rats were divided into 3 groups, each group consist of six animals. Group I orally administered with normal saline and served as control group. Group II and III received orally 100 mg/kg body weight of MFE and MLE respectively. After 30 min of extracts administration, 2 g/kg body weight of glucose was given orally to rats. Blood sample were taken from tip of the tail prior to glucose administration and at 30 min and 90 min after glucose loading.

Effect of extracts in alloxan-induced diabetic rats

Diabetes was produced in rats by the intraperitoneal administration of alloxan monohydrate (120 mg/kg, body weight). The blood glucose level was checked at 72 h after alloxan injection. Only those animals that showed blood glucose level between 170-300 mg/dl were used in experiment. Control group orally administered with normal saline. Group II served as positive control and orally administered with Tolbutamide (100 mg/kg, body weight). Group III and IV received 100 mg/kg body weight of MFE and MLE respectively. The treatment was continued once daily for seven days. At day 7 blood were collected from tip of tail for the estimation of blood glucose level.

Effect of extracts on body weight in alloxan-induced diabetic rats

Body weight of all animals was taken before alloxan injection and then at day 4 and day 7 of post-treatment by electronic balance (Electronic Scale, TH-1002).

Biochemical estimation

After blood glucose estimation on day 7, whole blood was collected by cardiac puncture under mild anesthesia from rats. Blood cholesterol, triglycerides and urea were evaluated in alloxan-induced diabetic rats by autoanalyser using Erba diagnostic Kits [30].

Statistical analysis

The results obtained were expressed as mean ± S.E.M. The statistical evaluations were made using ANOVA followed by LSD post hoc multiple comparison tests, in order to compare more than two groups. All data were processed with SPSS version no. 17 software. $P \leq 0.001$ was considered as significant.

RESULTS

Acute toxicity

Safety of the MFE and MLE was evaluated by oral administration up to 5 g/kg, body weight respectively. The extracts were found to be non-toxic and did not cause any mortality of the tested animals.

Effects on Fasting blood glucose (FBG) levels of Normal Rats

The effect of methanolic extracts of both the flower and leaves of *Mimusops elengi* Linn on fasting blood glucose levels of normal rats were depicted in (**Fig 1**). Oral administered of MFE and MLE at a dose of 100 mg/kg, body weight showed significant ($P < 0.01$) reduction in blood glucose level within 2 h.

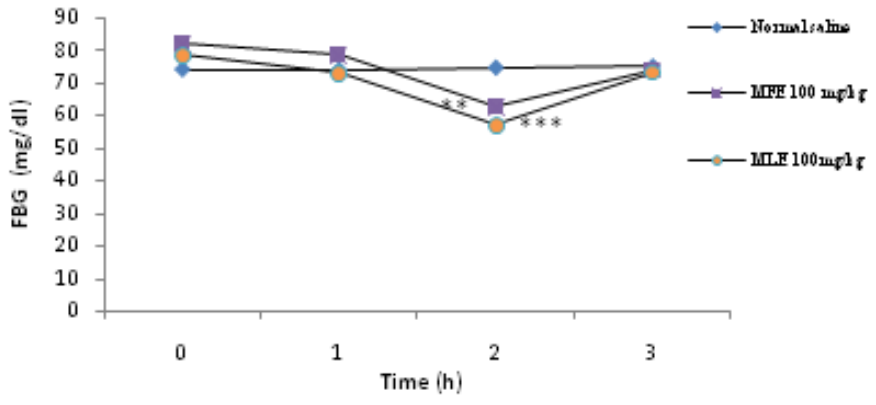

Fig 1: Effect of *Mimusops elengi* Linn leaves and flower extracts on Fasting blood glucose (FBG). Animals were pretreated by oral administration of MFE, MLE (100 mg/kg, body weight) and normal saline. Values were expressed as mean ± S.E.M (n=6). Statistical significance were calculated by ANOVA followed by LSD post hoc test * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ when compare to the control.

Oral glucose tolerance test (OGTT)

The oral glucose tolerance test in rats was showed in (**Fig 2**). The oral administrated of MFE and MLE (100 mg/kg, body weight) respectively prior to glucose loading (2 g/kg, body weight), significantly ($P < 0.001$) increased tolerance for glucose in all rats.

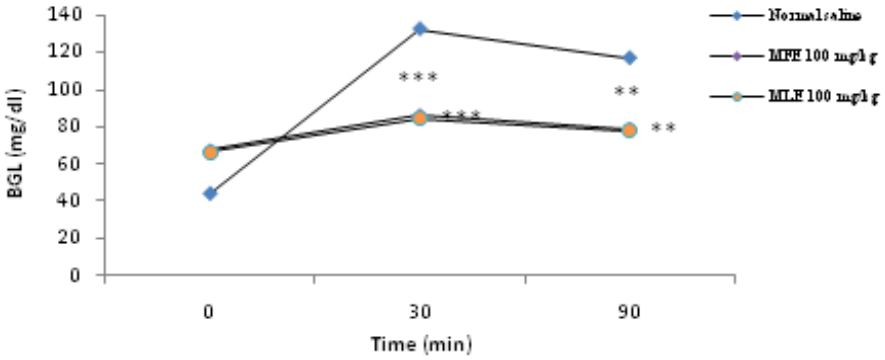

Fig 2: Effect of *Mimusops elengi* Linn leaves and flower extracts on oral glucose tolerance test (OGTT). Animals were pretreated by oral administration of MFE, MLE (100 mg/kg, body weight) and normal saline. Glucose 2 mg/kg, body weight were given after 30 min of extracts administration. Values were expressed as mean ± S.E.M (n=6). Statistical significance were calculated by ANOVA followed by LSD post hoc test * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ when compare to the control.

Effects on blood glucose level of Alloxan-induced Diabetic Rats

The effects of MFE and MLE on blood glucose level of alloxan-induced diabetic rats were showed in (**Table 1**). In diabetic control group, the blood glucose level was increased from 85.83to 205.66 mg/dl after alloxan injection. While the blood glucose level in alloxan-induced diabetic rats when treated with Tolbutamide, MFE and MLE (100 mg/kg, body weight) decrease from 209.16, 221.83, 210.50 to 108.0, 157.0, 173.33 mg/dl respectively. Significantly decreased ($P < 0.01$) in blood glucose level was observed in MFE and MLE when compare to Tolbutamide. The percentage reduction in blood glucose levels after seven days treatment with Tolbutamide and extracts was found to be 35.30%, 59.77% and 58.07% respectively.

Table 1: .Effects of extracts on blood glucose levels of Alloxan-induced diabetic rats.

Treatment groups	Dose (mg/kg)	Blood Glucose Level (mg/dl)				
		Pre-treatment	Post-treatment			
		Day 0	Day 4	%	Day 7	%
Diabetic Control	-	85.83±1.79	203.00±7.75	57.71	205.66±1.60	58.26
Tolbutamide	100	69.66±0.88	209.16±3.05	66.69	108.00±2.59***	35.50
MFE	100	63.16±1.30	221.83±3.73*	71.52	157.00±9.89***	59.77
MLE	100	72.66±2.33	210.50±2.51	65.48	173.33±11.21**	58.07

Animals were made diabetic with alloxan monohydrate (120 mg/kg, body weight) injection. After 72 h, animals showing blood glucose level between 170-300 mg/dl were oral administered with MFE, MLE (100 mg/kg, body weight), normal saline and Tolbutamide (100 mg /kg, body weight) respectively. Values were expressed as mean ± S.E.M (n=6). Statistical significance were calculated by ANOVA followed by LSD post hoc test * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ when compare to control.

Effects on body weight of Alloxan-induced Diabetic Rats

The body weight change in diabetic control and diabetic rats treated with Tolbutamide or with extracts (MFE and MLE) were summarized in (**Table 2**). Weight of the animals was taken at the start of the experiment and then at day 4 and day 7. MFE and Tolbutamide showed significant increase ($P < 0.001$) of body weight up to 5.24 %, 3.35% respectively after 7 days treatment period. While the animals treated with MLE showed significant ($P < 0.001$) reduction in their body weight.

Table 2: Effects of extracts on body weight of Alloxan-induced diabetic rats.

Treatment groups	Dose (mg/kg)	Body Weight (g)				
		Pre-treatment	Post-treatment			
		Day 0	Day 4	%	Day 7	%
Diabetic Control	-	154.50±1.85	145.83±1.30	-5.94	133.66±1.33	-15.59
Tolbutamide	100	144.16±1.04	146.33±1.22	+1.48	149.16±1.40***	+3.35
MFE	100	132.33±1.20	135.33±1.42**	+2.21	139.66±1.17*	+5.24
MLE	100	151.33±0.80	149.00±0.36	-1.56	146.66±0.80***	-3.18

Animals were made diabetic with alloxan monohydrate (120 mg/kg, body weight) injection. After 72 h, animals showing blood glucose level between 170-300 mg/dl were oral administered with MFE, MLE (100 mg/kg, body weight), normal saline and Tolbutamide (100 mg /kg, body weight) respectively. Initial weights of all rats were taken before treatment and then at day 4 and 7. Values were expressed as mean ± S.E.M (n=6). Statistical significance were calculated by ANOVA followed by LSD post hoc test * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Effects on Lipid and Blood Urea of Alloxan-induced Diabetic Rats

The effects on cholesterol, triglycerides and blood urea concentration compared to the diabetic control were illustrated in (**Table 3**). In diabetic rats, MFE and MLE treatment at a dose of 100 mg/kg, body weight for 7 days significantly ($P < 0.01$) decreased triglycerides levels compared to the diabetic control group. No significant difference was observed between MFE treated and diabetic control groups for cholesterol and MLE treated group for blood urea.

Table 3: Effects on Lipid and Blood Urea of Alloxan-induced Diabetic Rats

Treatments groups	Dose (mg/kg)	Cholesterol (mg/dl)	Triglycerides (mg/dl)	Blood Urea (mg/dl)
Diabetic Control	-	56.00±1.91	44.66±1.83	43.83±1.92
Tolbutamide	100	48.00±2.26*	33.83±2.68**	22.33±0.42***
MFE	100	57.16±2.91	32.33±1.60***	33.00±5.07*
MLE	100	48.66±1.25*	33.83±0.98***	44.83±2.30

After blood glucose estimation on day 7, whole blood was collected by cardiac puncture under mild anesthesia from rats. Values were expressed as mean ± S.E.M (n=6). Statistical significance were calculated by ANOVA followed by LSD post hoc test * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ when compare to control.

DISCUSSION

Diabetes mellitus is a disease caused by deficiency of insulin that results in increase blood glucose level and that leads to hyperglycemia. Over a period of time, this increase blood glucose affect other organ in the body like eye, kidney, brain and heart and develop complication like retinopathy, nephropathy, neuropathy and heart problems [31]. Alloxan is used as a cytotoxic agent to the insulin-secreting beta cells of pancreas and effectively produced diabetes in an experimental model [32]. Alloxan decreases endogenous release of insulin which results in increase blood glucose level in diabetic rats. The dose of alloxan used to partially destroy the pancreatic β-cells in alloxanized rats is 120 mg/kg, body weight.

Safety of the extracts was evaluated by oral administration up to 5 g/kg, body weight respectively. No visible signs of toxicity were observed in mice at this higher dose. Any substance estimated to be greater than 2000-5000 mg/kg, body weight could be considered being safe [33].

The present study was conducted in three experimental models i.e. normoglycaemic, acute hyperglycemia (OGTT) and chronic hyperglycemia (alloxan-induced diabetes). Both methanolic extracts of flower and leaves of *Mimusops elengi* Linn (100 mg/kg, body weight) produced significant ($P < 0.01$) reduction in blood glucose level within 2 h of oral administration in normal fasting rats. This indicated that dosage of 100 mg/kg MFE and MLE respectively could effectively decrease the fasting blood glucose levels in normal rats compared to the control group. The results of oral glucose test revealed that the extracts significantly low the elevated glucose level probably due to improved glucose utilization by the peripheral tissue [34]. The onset of action was found to be 30 min. Weight loss is one of the characteristic symptoms of diabetes. This weight loss is due to the increase break down of fats and tissue protein [35]. Improvement in the body weight of the treated animals might be due to better glycemic control as a result of the restoration of normal metabolism in muscle cells [34]. Usually, diabetes is associated with profound alteration in lipid profile [36]. Hyperlipidemia in diabetes increased the risk of micro and macrovascular disease and related complications [37]. The decreased in cholesterol and triglycerides by MLE might be directly or indirectly related with the decreased of blood glucose levels in alloxan-induced diabetic rats.

The exact mechanism through which the extracts reduce blood glucose level is not known. But this may probably due to increased sensitivity of insulin receptors or increase in the protective/inhibitory effect against insulinase enzyme [38]. Other mechanisms may involve improved glucose homeostasis. Increase of peripheral utilization of glucose, increase of synthesis of hepatic glycogen and/or decrease of glycogenolysis acting on enzymes, inhibition of intestinal glucose absorption, reduction of glycaemic index of carbohydrates, reduction of the effect of glutathione [39]. The present work proves the traditional claim associated with *M. elengi* not only for its antidiabetic activity but also hypolipidemic activity too.

CONCLUSION

In present study, the significant decrease in blood glucose level in normal and alloxan-induced diabetic rats in plant treated groups is a confirmation with the previously reported hypoglycemic effect of *M. elengi* bark and leaves extracts. Thus, it is evident that *Mimusops elengi* Linn could be prove as potent antidiabetic and hypolipidemic agent. Further studies are needed

to isolate the active constituents of plant that are involved in such activities.

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REFERENCES

1. Tanko Y, Yerima M, Yaro AH, Musa KY, Mohammad A. Hypoglycemic activity of methanolic stem bark of *Adansonnia digitata* extract on blood glucose level of streptozocin-induced diabetic Wister rats. International J. Applied Research in Natural Products (2008), 1(2): 32-36.
2. Mustafa A, Nilufer O, Didem DO, Fatma E**.** Hypoglycemic activity and antioxidant potential of some medicinal plants traditionally used in Turkey for diabetes. J. Ethanopharmacol (2010)**,** 128: 384-389
3. Kameswara RB, Kesavulu MM, Giri R, Appa Rao Ch. Antidiabetic and hpyolipidemic effects of *Momordica cymbalaria* Hook. Fruit powder in alloxan-diabetic rats. J. Ethanopharmacol (1999), 67: 103-109.
4. Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, Taskinen MR, Groop L. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabet Care (2001), 24: 683– 689.
5. Islam S, Islam R, Rahman M, Ali S, Mosaddik A, Sadik, G. Evaluation of antidiabetic activity of *Peltophorum pterocarpum* on alloxan and glucose induced diabetic mice. Inter J. Pharmaceutical Sci and Res (2011), 2(6): 1543-1547.
6. Sy GY, Cisse A, Nongonierma RB, Sarr M, Mbodj NA, Faye B. Hypoglycaemic and antidiabetic activity of acetonic extract of *Vernonia colorata* leaves in normoglycaemic and alloxan-induced diabetic rats. J. Ethanopharmacol (2005), 98: 171-175.
7. Marles RJ, Farnsworth NR Antidiabetic plants and their active constituents. Phytomedicine (1995), 2: 137-189.
8. Noor A, Gunasekaran S, Manickam AS, Vijayalakshmi MA. Antidiabetic activity of *Aloe vera* and histology of organ in stretozptocin-induced diabetic rats. Curr Sci (2008), 94 (8): 1070-1076.
9. Yasin JN. Flora of Pakistan, Pakistan Agriculture Research Council, Islamabad (1984), No.163, pp 1- 12.
10. Paranjpe P. Indian Medicinal Plants Forgotten Healers, Chaukhamba Sanskrit Pratishthan, Delhi, (2001), pp 37-38.
11. Nadkarni KM. Indian Materia Medica1, Vol I, Popular Prakashan Pvt. Ltd., Bombay (1986), pp 800-802.
12. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants, National Institute of Science Communication and Information Resources (CSIR), New Delhi (2000), pp 167.
13. Joshi SG. Medicinal Plants, Oxford & IBH publishing Co. Pvt. Ltd (2000), pp 362.
14. Narayan DP, Purohit SS, Sharma AK, Kumar T. Medicinal Plants, A complete source book, Agrobios, India (2003), pp 345.
15. Raveendra KR, Martin P. Ethanomedicinal Plants, Part II, Agrobios Publication, Jodhpur, India, (2006), pp 144.
16. Kapoor LD. Hand Book of Ayurvedic Medicinal Plants, CRC Press (2000), pp 232-233
17. Jahan N, Ahmed W, Malik A. Phytochemistry of genus *Mimusops*. J. Chem Soci Pak (1996), 18(1): 51-55.
18. Wong KC, Teng YE. Volatile Components of *Mimusops elengi*. J. Essential Oil Res (1994), 6(5): 453-458.
19. Gupta GK, Dhar KL, Atal CK. Chemical constituent of *Mimusops elengi* flower. Indian J. Chem (1976), 14B: 818.
20. Khare CP. Indian Medicinal Plants, Springer Publication, (2007), pp 416-417.
21. Jerline M, Jothi, G, Brindha P. Effect of *Mimusops elengi* Linn. bark extract on

alloxan induced hyperglycemia in albino rats. J Cell and Tissue Res (2009), 9(3): 1985-1988.

22. Ganu G, Jadhav S. In vitro Antioxidant and in vivo Antihyperglycemic potential of *Mimusops elengi* L. in alloxan-induced diabetes in mice. J. Complementary and Integrative Med (2010), 7(1): 1-13.
23. Ganu GP, Jadhav SS, Deshpande AD. Antioxidant and antihyperglycemic potential of methanolic extract of bark of *Mimusops elengi* L. in mice. Res J. Pharmaceutical, Biological and Chemical Sci (2010), 1(3): 67-77.
24. Mamatha MK, Tincy T, Yogesh HS, Pramod HJ. Antidiabetic activity of *Mimusops elengi* leaves on alloxan induced diabetic rats. Inter J. Pharma Sci (2011), 3(2): 1358-1362.
25. Jaffar S, Khakis SM, Brahma PN. Protective activity of ethanolic leaf extract of *Mimusops elengi* Linn on lipid peroxidation and antioxidant enzymes in experimental diabetic rats. Pharmanest- An Inter J Advances in Pharma Sci (2011), 2(2-3): 264-275.
26. Dr. Pandey G, Dravyaguna V, Varanasi. Oriental Publishers, (2011), pp 313- 317.
27. Lorke D. A new approach to practical acute toxicity testing. In: Archives of Toxicology (1983), 54 pp 275-287.
28. Vats V, Grover JK, Rathi SS. Evaluation of anti-hyperglycemic and hypoglycemic effect of *Trigonella foenum-graecum* Linn, *Ocimum sanctum* Linn and *Pterocarpus marsupium* Linn in normal and alloxanized diabetic rats. J. Ethanopharmacol (2002), 79: 95-100.
29. Joy KL, Kuttan R. Antidiabetic activity of *Picrrhiza kurroa* extract. J. Ethanopharmacol (1999), 167: 143-148.
30. Raifi N, Bachorik PP, Albers JJ. Lipids, lipoproteins and apolipoproteins. In C.A Burtis and E.R Ashwood, eds. Textbook of Clinical Chemistry, W.B Saunders Company, Philadelphia, (1999), pp 809-861.
31. Kumar S, Kumar V, Prakash O. Antidiabetic, hypolipidemic, and antioxidant activities of *Callistemon lanceolatus* leave extract. J. Herbs, Spices and Medicinal Plants. (2011), 17: 144-153.
32. Chika A, Bello SO. Antihyperglycaemic activity of aqueous leaf extract of *Combretum micranthum* (Combretaceae) in normal and alloxan-induced diabetic rats. J. Ethanopharmacol (2010), 129: 34-37.
33. Bruce RD. An Up and Down procedure for acute toxicity testing. Fundamental and Applied Toxicology (1985), 5 (1): 151-157.
34. Gulam MH, Paras NH, Rakesh KS, Vikas K. Antidiabetic activity of standardized extract of *Quassia amara* in Nicotinamide-Streptozocin-induced diabetic rats. Phytotherapy Res (2011), 25: 1806-1812.
35. Wadkar KA, Magdum CS, Patil SS, Naikwade NS. Antidiabetic potential and Indian Medicinal Plants. J. Herbal Med and Toxicology (2008), 2(1): 45-50.
36. Krentz AJ. Lipoprotein abnormalities and their consequences for patient with type II diabetes. Diabetes Obes. Metab (2003), 5 (Suppl. 1): S19-S27.
37. Brown BG, Zhao XQ, Sacco DE, Albers JJ. Lipid lowering and plaque regression. New insights into prevention of plaque disruption and clinical events in coronary disease. Circulation (1994), 87: 1781-1791.
38. Mostofa M, Choudhury ME, Hossain MA, Islam MZ, Sumon MH. Antidiabetic effects of *Catharanthus roseus*, *Azadirachta indica*, *Allium sativum* and Glimepride in experimentally diabetic induced rat. Bang J. Veterinary Med (2007), 5(1&2): 99-102.
39. Bnouham M, Ziyyat A, Mekhfi H, Tahri A, Lagssyer A. Medicinal plants with potential antidiabetic activity-A review of ten years of herbal medicine research (1990-2000). Inter J. Diabet and Metabolism (2006), 14: 1-25.