Available online on www.ijppr.com
International Journal of Pharmacognosy and Phytochemical Research 2017; 9(5); 689-693

ISSN: 0975-4873

Research Article

# Anti-Hyperglycemic and Anti-Hyperlipidemic Potential of the Leaves of *Maesobotrya dusenii* Hutchinson

Suleiman Mikailu, Kio Anthony Abo

*Department of Pharmacognosy and Phytotherapy, Faculty of Pharmaceutical Sciences, University of Port Harcourt, Nigeria*

***Received: 31st January, 17; Revised 27th April, 17, Accepted: 15th May, 17; Available Online:25th May, 2017***

**ABSTRACT**

Objective: To investigate the ethnomedicinal use of the leaves of *Maesobotrya dusenii* Hutchinson (Euphorbiaceae) in the treatment of diabetes mellitus. Methods: Powdered leaves were successively extracted with n-hexane, chloroform and 70% ethanol for three consecutive days respectively and the obtained extracts were assessed for phytochemicals, acute toxicity, anti-hyperlipidemic and anti-hyperlipidemic activity on albino rats. The acute toxicity was assessed by Lorke's method. Hyperglycemia was achieved by intraperitoneal injection of alloxan monohydrate (120mg/kg). Blood glucose was determined daily for seven days using a glucometer. On the seventh day of treatment, blood samples were obtained and the serum triglycerides (TG), total cholesterol (TC), glycosylated heamoglobin (GH), urea and high density lipoprotein (HDL) were determined. The active hexane fraction was further fractionated by column chromatography. Results: The phytochemical screening revealed the presence of terpenoids, phenolic compounds and carbohydrates. Death was not recorded at 5000mg/kg in the toxicity study. The n-hexane extract showed the highest significant ($p<0.05$) reduction of 74.1% in blood glucose which was comparable to Glibenclamide (79.7%). Further fractionation yielded six fractions (F1-F6) in which fraction F4, F5 and F6 were the most active with 83, 80 and 79% reduction of blood glucose. The lipid profile of the active fractions also exhibited decrease in TG, TC, GH, Urea and increase in HDL. Conclusion: This study reports for the first time, the acute toxicity, anti-diabetic and anti-hyperlipidemic potential of leaves of *Maesobotrya dusenii*. This study also justifies its ethno-medicinal use in the treatment of diabetes mellitus in Rivers State, Nigeria.

**Keywords**: *Maesobotrya dusenii, Euphorbiaceae, hyperglycemia, hyperlipidemia, acute toxicity.*

## INTRODUCTION

Diabetes is a chronic disease that is characterised by a relative lack of or insensitivity to insulin or both[1]. It is a multi factorial and heterogenous disorder with both genetic and environmental factors contributing to its development[2]. It is a disorder characterized by high blood sugar levels (hyperglyceamia) and presence of high sugar levels in the urine (glycosuria). The chronic disorder is associated with long term damage, dysfunction, and failure of various organs, especially eyes, kidneys, nerves, heart and blood vessels. Therefore, diabetes leads to reducing patient's quality of life and life expectancy.

*Maesobotrya dusenii* Pax is a notable species belonging to the Euphorbiaceae family. It is mostly found in the rain forest of Southern Nigeria, West and East Cameroun, Equitorial Guinea[3]. It is a tree or shrub of about 15 m high. The stem and root bark of *Maesobotrya dusenii* has been locally used to treat skin infections, spots, gonorrheae, dysentry in Akwa Ibom[4]. The stem of Maesobotrya dusenii is used for rural architecture, as building poles and trap pole[5]. The ripe fruits are also edible and are used to make jam[6]. The ethanolic extract of the stem bark of *Maesobotrya dusenii* showed significant antimicrobial activity against *Pseudomonas aeruginosa* and *Aspergilus flavus*[7]. There is paucity of scientific validation of the reported uses of this plant and its chemical constituent. However, the use of extracts of Maesobotrya dusenii by traditional medical practitioners to treat diabetes mellitus has necessitated this research work which is to investigate the antidiabetic activity of the leaf extracts of *Maesobotrya dusenii.*

## MATERIALS AND METHODS

*Plant Material*

*Maesobotrya dusenii* leaves were collected from Etche area in River State. The fresh leaves were identified and authenticated by Dr. N. L. Edwin-Wosu at Plant Science and Biotechnology Herbarium, University of Port Harcourt and a herbarium specimen was deposited at the Herbarium of the Department of Pharmacognosy and Phytotherapy, Faculty of Pharmaceutical Sciences, University of Port Harcourt. The leaves were air-dried at room temperature and pulverized and kept in an airtight container for analysis.

*Extraction*

A 1kg of the dried powdered leaves of *M. dusenii* was successively macerated with n-hexane, chloroform and 70%ethanol for 3 days consecutively. The combined filtrate of each of the solvent was evaporated *en vacuo* in a rotary evaporator at 40°C and weighed. The extracts were

**Author for Correspondence: slymeek01@yahoo.com*

Table 1: Effect of n-hexane, chloroform and aqueous ethanol extract of *M. dusenii* on blood glucose level of alloxan-induced hyperglycemic rats.

| Group | Day 1 | | | | Day2 | Day3 | Day4 | Day5 | Day6 | Day7 |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 minutes | 60 minutes | 120 minutes | 180 minutes | | | | | | |
| Normal | 118.00 ±3.79 | 118.00 ±3.78 | 128.67 4.26 | ±119.00 ±6.11 | 142.00 ±36.00 | 120.30 ±3.33 | 134.00 ±7.55 | 113.00 ±7.42 | 118.00 ±7.42 | 127.67 ±7.33 |
| Diabetic Control | 227.00±17.95 | 283.33±7.26 | 255.00±22.06 | 383.33±100.84 | 235.70 ±3.8 | 255.00 ±21.7 | 361.33 ±21.17 | 350.00 ±120.33 | 422.67 ±32.79 | 529.00 ±58.40 |
| Glibenclamide (2.5mg/kg) | 255±73.71 | 217.30±29.14 (23.29) | 190.33±45.88 (25.49) | 192.67±53.16 (49.73) | 158.00 ±36.53 (32.97) | *124.67 ±12.83 (51.10) | *180.33 ±24.67 (50.09) | 205.00 ±7.57 (41.43) | *135.33 ±25.77 (67.98) | *107.30 ±3.92 (79.72) |
| n-hexane (1g/kg) | 246.30±19.35 | 233.30±17.52 (17.66) | 251.00±32.23 | 248.80±31.75 (35.11) | 249.80 ±32.04 | 241.80 ±3.76 (5.2) | *185.00 ±17.05 (48.8) | *167.30 ±3.78 (52.19) | *123.50 ±5.23 (70.8) | *137.20 ±9.04 (74.06) |
| Chloroform extract (1g/kg) | 233.67±18.59 | 344.33±12.85 | 365.67±11.22 | 295.67±13.84 (22.87) | 280.70 ±56.12 | 290.30 ±50.84 | 321.00 ±21.17 (11.2) | 294.00 ±82.07 (16) | 289.30 ±69.54 (31.03) | 267.00 ±69.34 (49.52) |
| Ethanol extract (1g/kg) | 212.80±18.58 (6.2) | 192.5±23.85 (32.06) | 210.0±11.36 (17.64) | 240.00±5.77 (37.39) | 237.70 ±28.36 | *130.30 ±14.56 (48.9) | *197.30 ±25.73 (45.39) | *192.30 ±22.72 (45.1) | *203.00 ±25.65 (52.0) | *182.30 ±22.00 (62.5) |

*Each value is represented as mean ± S.E.M. The figures in parenthesis indicate the % decrease in blood glucose level.*represents the values significantly different from the control ($p \leq 0.05$)*

subjected to bioassay and toxicity screening.

*Phytochemical Screening*

Phytochemical screening was performed on the powdered leaves and extracts to detect the presence of secondary metabolites using standard procedures[8] and[9].

*Column Chromatography*

The bioactive n-hexane extract was fractionated on column chromatography packed with silica gelG (60-120 mesh), eluted with gradient mixtures of n-hexane, dichloromethane and methanol. Fractions were monitored on pre-coated analytical thin layer chromatography (TLC) $GF_{254}$, developed in dichloromethane. Six fractions (F1 to F6) were obtained and tested separately on experimental animal models (biological assay).

*Experimental Animals*

Healthy adult Wistar male and female rats weighing between 150-200g were obtained from the animal house of the Department of Experimental Pharmacology Toxicology, Faculty of Pharmaceutical sciences, University of Port Harcourt, Rivers State. The rats were fed on standard feed (from Premier feed mills, Rivers State) and water *ad libitum.* All experimental animals were housed in metabolic cages in a well ventilated room for a two-week period of acclimatization.

*Acute toxicity evaluation*

A total of 18 albino rats of either sex weighing 150-200 g were used in the determination of the acute toxicity of the leaf extract of *Maesobotrya dusenii*. The rats were randomly divided into six groups of three (3) rats each and the first group was given 10mg/kg, the second group 100mg/kg and the third group 1000mg/kg of the plant extract respectively via the oral route. The rats were observed for signs of toxicity, adverse effects or death. After 24 hours, the second three groups of rats were given 1600, 2900 and 5000 mg/kg of the plant extract respectively and observations were noted as previously described[10].

*Alloxan-induced hyperglycemic assay*

Rats were divided into six groups of five rats each. Rats in cages 2-6 were fasted overnight and hyperglycemia was induced by a single intraperitoneal injection of 120 mg/kg alloxan monohydrate solution. The rats became diabetic within 3days. Rats in cage 1 were the normal (untreated) while the cage 2 consisted of untreated (but given tween 80 which was used to dissolve the hexane and chloroform extract) diabetic rats. Cage 3 contained diabetic rats treated with glibenclamide (2.5mg/kg), cages 4 - 6 consisted of diabetic rats treated with n-hexane, chloroform and aqueous ethanol extract at 1g/kg respectively. Blood glucose was determined at intervals and daily as previously described[11].

*Sample Collection*

At the end of the experiment, rats in the most active group and the controls were sacrificed under anesthesia and blood was collected by cardiac puncture into EDTA bottles and centrifuged to obtain serum.

*Biochemical Analysis*

The biochemical analysis of serum samples was performed using reagents kits (Randox Kits, Randox Laboratories, UK). Biochemical parameters measured were serum triglycerides (TG), total cholesterol (TC), high density lipoprotein (HDL), urea, and glycosylated hemoglobin (HbA1c%).

*Statistical Analysis*

All data obtained from the study were expressed as mean ± SEM. The significant differences between the mean of the treated and the control animals were established by student's t-test.

Table 2: Effect of n-hexane fractions of *M. dusenii* on blood glucose level of alloxan-induced hyperglycaemic rats.

| Groups | Day 1 | | | | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 min | 60min | 120min | 180min | | | | | | |
| Normal | 78.00±0.47 | 82.56±0.67 | 71.45±1.03 | 68.00±0.82 | 86.67±1.66 | 79.33±0.42 | 85.70±2.05 | 78.00±2.16 | 81.32±0.85 | 77.00±1.25 |
| Diabetic Control | 538.00±0.94 | 554.00±3.00 | 558.00±1.69 | 587.00±7.58 | 513.60±0.47 | 540.00±3.40 | 582.00±1.25 | 524.00±0.47 | 566.00±1.25 | 578.00±1.41 |
| Glibenclamide (2.5mg/kg) | 462.33±1.65 | 306.00±3.09 (44.76) | 332.00±1.69 (40.50) | *228.00±1.69 (61.15) | *283.00±7.94 (44.89) | *249.33±8.99 (53.83) | *213.33±3.53 (63.35) | *190.33±7.53 (63.68) | *167.67±2.60 (70.38) | *154.33±3.79 (73.30) |
| Fraction1 (200mg/kg) | 532.00±1.25 | 545.00±1.41 | 561.00±2.16 | 580.00±1.70 | 527.00±1.25 | 569.00±0.94 | 586.00±2.63 | 546.00±2.49 | 541.00±2.06 | 570.00±4.54 |
| Fraction2 (200mg/kg) | 552.00±1.70 | 523.00±2.45 | 466.00±1.25 | 451.00±0.81 | 567.00±2.06 | 559.00±1.69 | 561.00±0.81 | 479.00±0.81 | 498.00±3.56 | 469.00±2.94 |
| Fraction3 (200mg/kg) | 431.00±1.25 | 410.00±0.47 (25.99) | 376.00±1.25 (32.62) | 343.00±0.94 (41.57) | 340.00±2.05 (33.80) | 351.00±1.69 (35.00) | *320.00±0.94 (45.00) | *272.00±2.63 (48.09) | *196.00±3.74 (65.37) | *161.00±2.49 (72.15) |
| Fraction4 (200mg/kg) | 386.00±0.47 | *185.00±0.94 (66.61) | *153.00±0.94 (72.58) | *123.00±0.47 (79.00) | *125.00±0.94 (75.66) | *129.00±1.25 (76.11) | *120.00±0.47 (79.38) | *177.00±2.06 (66.22) | *102.00±1.41 (81.98) | *95.00±0.82 (83.56) |
| Fraction5 (200mg/kg) | 436.00±2.16 | 386.00±1.88 (30.32) | *256.00±0.47 (54.12) | *201.00±0.47 (65.75) | *203.00±0.74 (60.42) | *179.00±1.25 (66.85) | *177.00±0.81 (69.59) | *147.00±1.25 (71.95) | *133.00±2.94 (76.50) | *110.00±2.05 (80.97) |
| Fraction6 (200mg/kg) | 541.00±0.81 | 533.00±1.41 | 466.00±5.99 (16.48) | 399.00±0.94 (32.00) | 385.00±1.25 (25.04) | 359.00±0.94 (33.52) | 361.00±2.16 (37.97) | *205.00±2.49 (60.88) | *133.00±1.63 (76.50) | *121.00±2.62 (79.07) |

*Each value is represented as mean ± S.E.M. The figures in parenthesis indicate the % decrease in blood glucose level.*represents the values significantly different from the control($p \leq 0.05$)*

## RESULTS

*Yield of extract from 1kg of plant material*

From 1kg of powdered material, 13.2g, 18.2g and 8.6g of extracts were obtained from hexane, chloroform and aqueous ethanol respectively. The phytochemical screening revealed the presence of saponins, terpenoids, cardenolides and carbohydrates while alkaloids, tannins and athraquinones were absent from the extracts.

*Effect of acute toxicity evaluation of M. dusenii*

The grouped rats that were given 10, 100, 1000, 1600, 2900 and 500mg/kg did not show any toxic symptoms and mortality was not recorded.

*Effect of hexane, chloroform and 70% ethanol extract of M. dusenii on blood glucose level of alloxan-induced hyperglycemic rats*

On day 1, within the interval of 0 and 180 minutes as shown in Table 1, none of the extracts produced significant reduction in blood glucose within the 180 minutes. However, the hexane extract showed significant reduction in blood glucose from day 4 with a peak of 74.06% on day 7. Chloroform extract did not show any reduction in blood glucose. The 70% ethanol extract exhibited a steady reduction in blood glucose from day 3 (48.9%) with a peak of 62.5% on day 7.

*Effect of fractions from hexane extract of M. dusenii on blood glucose level of alloxan-induced hyperglycemic rats*

In Table 3, Fractions 1 and 2 did not show any reduction in blood glucose of the rats from day 1 to day 7. Fraction 3 showed significant reduction from day 4 and with a peak reduction of 72.15% on day 7. Fraction 4 exhibited significant reduction from the 60 minutes of administration on day 1 to day 7 with a peak of 83% reduction. Fraction 5 also exhibited significant reduction from the 120 minutes

Table 3: Lipid profile of diabetic rats treated with active fractions from n hexane extract of *M. dusenii* on day 7

| | Normal | Diabetic untreated | Diabetic+ Glibenclamide | Diabetic+ fraction4 | Diabetic + Fraction 5 | Diabetic+ Fraction 6 |
|---|---|---|---|---|---|---|
| HBA1C(%) | 5.10±0.06 | 10.20±0.08 | 5.80±0.96 (43.14)[a] | 5.40±0.14 (47.06) [a] | 5.70±0.97 (44.12) [a] | 5.90±0.66 (42.16) [a] |
| TC (mg/dl) | 32.00±2.10 | 38.80±1.61 | 34.50±12.02 (11.08) [a] | 28.00±3.80 (27.84) [a] | 29.60±14.96 (23.71) [a] | 31.00±3.35 (12.10) [a] |
| TG(mg/dl) | 16.90±0.08 | 56.10±13.30 | 24.00±1.15 (57.22) [a] | 22.60±0.86 (59.72) [a] | 25.00±15.64 (55.44) [a] | 26.70±22.85 (52.41) [a] |
| HDL(mg/dl) | 41.60±3.39 | 28.80±2.65 | 33.20±10.68 (13.25)[b] | 37.10±0.08 (22.37) [b] | 38.9±11.20 (25.96) [b] | 31.00±0.12 (7.10) [b] |
| UREA(mg/dl) | 35.60±1.33 | 316.80±2.31 | 38.70±6.39 | 37.90±0.58 | 39.90±1.80 | 40.30±5.64 |
| VLDL(mg/dl) | 4.10±1.73 | 6.50±3.46 | 4.30±2.03 (33.85) [a] | 3.80±7.32 (41.54) [a] | 3.70±2.65 (43.1) [a] | 4.80±6.01 (26.15) [a] |
| LDL(mg/dl) | 21.23±2.66 | 34.70±4.16 | 22.70±5.12 (34.58) [a] | 18.90±1.77 (45.53) [a] | 19.60±4.54 (43.52) [a] | 21.50± 0.88 (38.04) [a] |

*Each value is represented as mean SEM of 5 rats, values in parenthesis with superscript a represent % decrease, superscript b represent % increase; * represents value that are significant (p<0.05); HBA1C= Glycosylated haemoglobin, TG=Triglyceride; TC=Total cholesterol; VLDL=Very Low Density Lipoprotein; HDL=High density lipoprotein; LDL=Low Density Lipoprotein*

of administration to day 7 with a peak of 87% reduction in blood glucose. Fraction 6 showed significant reduction from day 5 with a peak reduction of 79.07% on day 7.

*Effect of the active fractions from hexane extract of M. dusenii on the lipid profile of diabetic rats*

In Table 4, fraction 4 showed the highest percentage decrease in HbA1c%, TC, TG, and LDL in the rats among other fractions while fraction 5 exhibited the highest increase in HDL. The urea of the diabetic rats treated with F4, F5, and F6 revealed 37.9, 38.9 and 31.0 respectively while the untreated group of rats was 316.8mg/dl

## DISCUSSION

The search for safer, specific and effective hypoglyceamic agents has continued to be an important area of investigation with natural extracts from readily available traditional medicinal plants offering great potential for discovery of new antidiabetic drugs[12]. The phytoconstituents detected in the leaves of *M. dusenii* were the same as what was reported present in the root and stem bark[7] and[13]. The acute toxicity studies carried out on the aqueous ethanolic extracts of *M. dusenii* Pax at the dose level of 5000mg/kg body weight did not exhibit any adverse effect, toxic symptoms or lethality and therefore considered to be safe[14].

It could be observed from the result that the extracts did not have any effect from day 1 of administration but on further administration aqueous ethanol and hexane extract were able to decrease the blood glucose significantly from day 3 and 4 respectively. Hexane extract showed highest percentage reduction in the blood glucose of the rats and therefore became the choice for further separation on column chromatography which yielded six pooled fractions based on their thin layer chromatographic pattern. Table 3 revealed that out of the six fractions obtained from hexane extract, three (F4, F5 and F6) were biologically active. They significantly reduced the blood glucose of hyperglycemic rats by 83, 80 and 79% respectively. The reduction pattern of the fractions were similar to that observed in the glibenclamide which may suggest that the fractions were possibly stimulating the secretion of insulin from residual pancreatic beta cells as the glibenclamide though subject to experimental investigation. More so, the bioactive fractions tested positive to terpenoids by Liebermann Buchard test[9]. However, β-amyrin, a triterpenoid was reported to have been isolated from *Maesobotrya barteri* though the activity was not investigated[15]. Certain triterpenoids and steroids such as α-sistosterol-D-glycoside from *Ficus glomerata* and charantin from *Momordica charantia* have been reported to have antidiabetic activity[16] and[17].

Cardiovascular diseases are secondary complications of diabetes mellitus and are majorly from the risk of elevated plasma cholesterol and triglyceride level[18]. Existing antihyperglycemic agents control blood glucose levels with insufficient correction of lipid abnormality, especially in hypertriglyceridemia. The lipid profile result indicates that the bioactive fractions reduced the elevated triglyceride and elevated the low HDL significantly in such a way that correlates with the manifested reduction observed in the blood glucose of the hyperglycemic rats. This simply implies that the fractions controlled hyperglycemia and imbalance in lipid profile which can lead to cardiovascular diseases. However, similar hypolidemic effects have been reported in *Ocimum basilicum*[19], *Chamaerops humilis* leaves[20], and *Carica papya*[21] but not as effective as *M. dusemii*. Consequently, the sharp reduction in blood urea of the rats treated with the bioactive fractions were in the same range with the normal untreated rats while that of the diabetic untreated was very high indicating that the bioactive fractions have the potential of preventing the risk of renal failure in the rats.

## CONCLUSION

The study revealed the safety of the aqueous ethanolic extract of *Maesobotrya dusenii* due to the survival of the animals even at a dose of 5000mg/kg. The n-hexane extract

of *M. dusenii* showed anti-hyperglycemic activity and its fractions also showed more potent activity. The anti-hyperlipidemic activity of the fractions obtained from the hexane extract of *M. dusenii* was also exhibited by this investigation. However, further work is ongoing to characterized the anti-hyperglycemic principles of the leaves in a dose dependent response. Therefore, this study reports for the first time the phytochemical constituents, acute toxicity, antidiabetic and anti-hyperlipidemic activity of the leaves of *Maesobotrya dusenii* which also justifies the use of *Maesobotrya dusenii* in the management of diabetes mellitus by traditional medical practitioners.

**ACKNOWLEDGEMENT**

The authors are thankful to Dr. Afieroho OE and Pharm. B.A. Adewoyin of the Department of Pharmacognosy and Phytotherapy, Pharmacist Mayaki DS and Pharmacist Wosu JI.

**REFERENCES**

1. A. Cimbiz, Y. Ozay, N. Yurekdeler, K. Cayci, T. Colak, C.C. Aksoy & H. Uysa the effect of long-term exercise training on the blood glucose level and weight in alloxan administered mice *Sci Res Essay 2011; **6**(1):66-70*
2. Y. Hsieh, C. Chang, K. Hsu, F. Tsai, C. Chen & F. Tsai Effect of exercise training on caplain systems in lean and obese Zucker rats *Int J Biol Sci* 2008; 4:300-308.
3. A.R Walker & R.Sillans 1961: Les plantes utiles du Gabon. Paris: 170.
4. K.K. Ajibesin, D.N Bala, B.A.J. Ekpo & S.A. Adesanya Toxicity of some plants implicated as poisons in Nigerian ethnomedicine to rats *Nig J Nat Prod Med 2002; 6:7-9*
5. A.G.N. Fongod, L.M Ngoh & M.C. Veranso Ethnobotany, indigenous knowledge and unconscious preservation of the environment: An evaluation of indigenous knowledge in South and South West Regions of Cameroon *Int J Biodiversity and Conservation 2014;**6**(1):85-89*
6. Tolu Odugbemi A textbook of Medicinal Plants University of Lagos Press 2008
7. Uduak A. Essiet & Kola K. Ajibesin Antimicrobial activities of some Euphorbiaceae Plants used in the traditional medicine of Akwa Ibom State of Nigeria *Ethnobotanical leaflets. 2010; 14:654-64*
8. A. Sofowora 1993 Medicinal Plants and Traditional Medicine in Africa 2nd Edition, Spectrum Books Ltd, Sunshine House Ibadan Nigeria *1993: 134-156*
9. J.B. Harbourne Phytochemical methods 3rd edition Chapman and Hall; London.1998
10. D. Lorke 1983 A new approach to practical acute toxicity test *Arch Toxicol 1983: 275-287*
11. K.A. Abo & T.B. Jimoh Anti-hyperglycemic potential of stem bark of *Bauhinia monandra* Kurz in rats *Nig J Nat Prod Med 2004; 8:48-51*
12. B. Patwardhan, A.D.B. Vaidya & M. Chorghade Ayurveda and natural products drug discovery *Current Sciences 2004; **86**(6): 789-799*
13. Ntie-Kang F, Mbah F.J.A, Mbaze L.M, Lifongo L.L, Scharfe M, Hanna J.N *etal.* CamMedNP: building the Cameroonian 3D structural natural products database for virtual screening. *BMC Complement Altern Med 2013;13:88* PMID:23590173 PMCID:PMC3637470 DOI:10.1186/1472-6882-13-88
14. A.A. Adeneye & J.A. Olagunju Preliminary hypoglycemic activities of the aqueous seed extract of *Carica papaya* Linn in wistar rats *Biology and Medicine 2009;1 (1): 1-10*
15. Ogwuche CE, Amupitan JO, Ndukwe G & Ayo RG Isolation and Biological activity of the triterpene β-amyrin frm the aerial parts of *Maesobotrya barteri* (Baill) *Med Chem 2014; 4:729- 733*
16. P. Daisy, R. Jasmine, S. Ignacimuthu & E. Murugan A novel steroid isolated from *Elephantopus scaber* an ethnomedicinal plant with antidiabetic activity *J Phytomedicine 2009; **16**(2): 252-257*
17. A.A. Fred-Jaiyesimi, M.R. Wilkins and K.A. Abo Hypoglycaemic and amylase inhibitory activities of leaves of *Spondias mombin* Linn *Afri J Med Med Sci 2009; 38: 343-349*
18. Wen J.H, Zhong Y.Y, Wen Z.G, Kuang C.Q, Liao J.R, Chen LH1 *et al*, Triglyceride to HDL-C ratio and increased arterial stiffness in apparently healthy individuals *Int J Clin Exp Med. 2015 Mar 15;8(3):4342-8. eCollection 2015*
19. N.A. Zeggwagh, T. Sulpice, M. Eddouks Antihyperglycemic and hypolipidemic effects of *Ocimum basilium* aqueous extract in diabetic rats *Am J Pharmacol Toxicol. 2007;2:123–9*
20. F. Gaamoussi, Z. Israili, B. Lyoussi Hypoglycemic and hypolipidemic effects of an aqueous extract of *Chamaerops humilis* leaves in obese hyperglycemic and hypolipidemic Meriones shawi rats *Pak J Pharm Sci. 2010;23:212–9*
21. Yasmeen Maniyar and Prabhu BhixavatimathAntihyperglycemic and hypolipidemic activities of aqueous extract of *Carica papaya* Linn leaves in alloxan-induced diabetic rats *J Ayurveda Integr Med 2012**:3**(2); 70-74*