Hypolipidemic Effects of Aqueous Extract of Three Cultivars of *Musa sapientum* Fruit Peel on Poloxamer-407 Induced Hyperlipidemic Wistar Rats.

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ABSTRACT

Objective: The effect of aqueous extracts of the ripped fruit peel of three cultivars of *Musa sapientum* (Saro, Ominni and Oranta) on the lipid profile of normolipidemic and hyperlipidemic rats were examined.

Methods: Aqueous peel extracts of the 3-cultivars of *Musa sapientum* (100mg/Kg bw) were administered to normolipidemic and poloxamer-407 induced hyperlidemic rats (140-180g). Atorvastatin was used as standard drug (70 mg/Kg bw). Blood samples were collected for determination of plasma total cholesterol (Tc), triacylglycerides (TAG), low-density lipoprotein cholesterol (LDL-c) and high-density lipoprotein cholesterol (HDL-c) after 21-days in normolipidemic rats and 3-days in hyperlipidemic rats.

Results: Normolipidemic rats treated with extract of Saro showed a significant ($p<0.05$) increase in LDL-c. The extract treated hyperlipidemic rats showed a significant ($p<0.05$) reductions in the lipids. Animals treated with Oranta extract shows significant ($p<0.05$) reduction in serum Tc and TAG when compared to other peel extract treated groups but shows no significant ($p>0.05$) difference when compared to the Atorvastatin and normal control groups.

Conclusion: The findings in this study reveals Oranta cultivar of *M. sapientum* as a better potential drug candidate among the cultivars studied, hence could be useful for the treatment of hyperlipidemia and other cardiovascular related diseases.

Key words: *Musa sapientum*, poloxamer-407, hyperlipidemia, atherosclerosis, cardiovascular-disease.

Introduction

Hyperlipidemia has been rated as a major contributing factor underlying the development of several atherosclerosis diseases affecting the quality of human lives [1,2,3,4,5]. It is an elevation of one or more of the plasma lipids, including cholesterol, cholesterol esters, triglycerides and phospholipids [5,6]. An elevation of plasma lipids may primarily be due to genetic defect or secondarily to diet, drugs or diseases [1]. Hyperlipidemia promotes human atherosclerosis and is a risk factor for developing cardiovascular diseases (CVDs) [6]. Predominant CVDs associated with hyperlipidemia are hypertension, ischemic heart diseases, stroke, coronary heart diseases (CHDs) and atherosclerosis. They account for at least 80% of the burden of CVD in both developing and developed countries [7]. A 20% reduction of blood cholesterol level can decrease about 31% of CHD incidence, and 33% of its mortality rate [3].

It is well known that dietary factor, nutritional habits and genetic origin influence the risk of CVD. However, there are also increasingly evident that certain chemicals, such as surface-active agents (detergents) have the potential to cause hyperlipidemia [8,9]. One such example, Poloxamer-407 (P-407), has been shown to cause significant elevations in plasma cholesterol and triglycerides in various animal models, including rats [8]. Disease study in a suitable animal model is a classical approach towards the development of a credible therapeutic strategy for possible cure or management of the disease [9]. Hyperlipidemic rat models are extensively used in lipid research [2,3,6]**.**

Musa sapientum belong to the Kingdom: *Plantae*, division: *Magnoliophyta*, class: *Liliopsida*, Order: *Zingiberales*, family: *Musaceae*, Genus: *Musa*, species: *Musa sapietum. Musa* sapientum originated mainly from intra-and interspecific hybridizations between two wild diploid species, *M. acuminate* Colla ('A' genome) and *M. balbisiana* Colla ('B' genome) [10]. The cultivated varieties can present different genomic combinations: AA, AB, AAA, AAB, ABB, AAAA, AAAB, AABB and ABBB, diploids, triploids and tetraploids This depends on the basic number of chromosomes: two, three or four, respectively, being eleven, the basic number of chromosomes of the species [11]. For the purpose of this research work, only three of the

genomic combinations were used which are the once distributed within Nigeria. The cultivars are AA, AAB and ABB. Locally they are called “Saro”, “Paranta/Oranta” and “Amina/ominni” respectively.

M. sapientum fruit peels are used in Northern part of Nigeria for the treatment of hypertension and other cardiovascular related diseases. However, very little research has been done to determine the efficacy of this fruit peel in the treatment of CVD risk factors. Since elevated blood lipid levels are associated with CVD. It becomes pertinent to determine the efficacy of this fruit peels in the treatment of hyperlipidemia in order to justify its use among Northern Nigerians in treating CVD related diseases. It is our belief that this investigation will take us another step forward in our quest to understand the mechanism of action of *M. sapientum* in prevention and treatment of arteriosclerosis and heart related diseases.

MATERIAL AND METHODS

Plant samples collection and identification

The ripe Banana fruit peels of species (cultivars); Saro, Oranta and Ominni were collected from natural habitat within Zaria area of Kaduna State Nigeria. It was identified at the herbarium unit of Biological Sciences Department, Ahmadu Bello University, Zaria Nigeria.

Experimental animals

Forty-five wistar albino rats of both sexes weighing 140-180g were purchased from the Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria-Nigeria. They were housed in polypropylene cages in a room where the congenital temperature was 27°C ± 1°C and 12 hours Light and dark cycles were maintained. The animals were allowed to acclimatize to the environment for fourteen days and supplied with a standard pellet diet and water *ad libitum.*

Ethical Consideration: The study was conducted in accordance with the Ethical Committee Guidelines of the Institution on the use of animals for research.

Experimental Duration: The research study was conducted between November 2012 and August, 2013.

Preparation and extractions of plant

The banana peels were air-dried in the laboratory for a period of two weeks and were made into powder by grinding and were sieved with a mesh size of 0.05 mm. The banana peels aqueous extracts were prepared by soaking 300 g of the powdered in 1500ml (1:5) distilled water in 2 litres conical flask. It was stirred and allowed to stand for 48 hours. The extracts were thereafter filtered with filter paper. The filtrates were concentrated to dryness on a water bath set at 45^0C.

Acute toxicity (LD50) test

The mean lethal dose of aqueous peel extracts of Oranta, Ominni and Saro of *M. sapientum* were determined in albino rats using the method described by Lorke [12].

Preparation of standard drug

Atorvastatin (Pfizer Ireland pharmaceuticals, Ireland) was purchased in a tablet form at strength 20 mg. Tablets were crushed into powder, dissolved in distilled water and administered orally *ad libitum*.

Induction of hyperlipidaemia

A dose of 1.0 g/kg of P-407 (BASF Corporation; Mount Olive, NJ, USA) was introduced intraperitoneally. All syringes were placed on ice prior to P-407 administration to maintain the polymer in a mobile viscous state during the injection [13].

Animal grouping and treatment

A total of 45 rats were used. The rats were divided into 9 groups of 5 rats each as follows:

Group A (normolipidemic**)**

Group I: Normal control received feed and distilled water only for 21 days.

Group II: Normal rats treated with Saro 100 mg/kg bw/day aqueous extract orally for 21 days

Group III: Normal rats treated with Ominni 100 mg/kg bw/day aqueous extract orally for 21 days

Group IV: Normal rats treated with Oranta 100 mg/kg bw/day aqueous extract orally for 21 days

Group B (hyperlipidemic**)**

Group V: Hyperlipidemic control (HC) without treatment.

Group VI: were induced and given Atorvastatin at 70 mg/kg body weight for 3 days**.**

Group VII: Were induced and treated with aqueous extract of Saro (100mg/kg/b.wt/day) for 3 days**.**

Group VIII: Were induced and treated with aqueous extract of Ommini (100mg/kg/b.wt/day) for 3 days**.**

Group IX: Were induced and treated with aqueous extract of Oranta (100mg/kg/b.wt/day) for 3 days**.**

Blood Sample *Collection*

At the end of the experimental period, the rats were sacrificed by anesthesia using chloroform before sample collection. Blood was collected into EDTA bottles after decapitation and centrifuged, to obtain the plasma which was used for lipid analysis.

Plasma lipid analysis

The plasma samples were analyzed for total cholesterol (Tc), triglycerides (TAG) and high-density lipoprotein cholesterol (HDL-c). They were determined by enzymatic methods as described by Stein [14]. Low-density lipoprotein cholesterol (LDL-c) was calculated using Friedewald formula:

LDL-c = Tc – TAG / 5 – HDL-c

Data analysis

Data obtained were expressed as mean ± SD. The data were statistically analyzed using analysis of variance (ANOVA). The difference between the various extracts and animal groups were compared using the Duncan Multiple Range Test. The values of $p < 0.05$ were considered as significant.

Results

Changes in lipoprotein level

The lipid profile of normolipidemic and hyperlipidemic wistar rats administered extracts of *Musa sapientum* are shown in table 1 and 2 respectively. The results show that in normolipidemic rats (groups A) there were no significant ($p > 0.05$) change in the levels of Tc, TAG, LDL-c and HDL-c of the treated groups when compared to the normal control except the group treated with peel extract of Saro which recorded a significant ($p<0.05$) increase in LDL-c (80.50±14.85) when compared to the normal control (39.65±11.38), Oranta (17.13±3.59) and Ominni (31.85±7.28) peel extracts. Among the hyperlipidemic control group, there was significant ($p<0.05$) increase in the serum levels of Tc (446.53±27.57), TAG (743.45±18.77) and LDL-c (214.50±10.61) when compared to normal control and treated groups. Total cholesterol and TAG level in the hyperlipidemia control group increased by more than 5-folds and 12-folds respectively when compared to the normal control group. The serum TAG (289.70±18.87) and LDL-c (178.00±11.31) of Saro and TAG (273.44±18.90) and LDL-c (158.35±14.04) of animals treated with Ominni extract shows a significant ($p<0.05$) increase when compared to other treated groups. Animals treated with Oranta extract recorded the highest reduction ($p<0.05$) in serum total cholesterol (134.35±19.86) when compared to other extract treated groups but no significant ($p>0.05$) difference when compared to the standard drug (156.00±16.70) and normal control (84.50±9.19). Only the animals treated with the standard drug had significant ($p<0.05$) increase in the serum level of HDL-c (46.60±7.50) when compared to hyperlipidemia control (25.93±4.39) but there were no significant ($p>0.05$) difference among other treated groups and the normal control.

Table 1: EFFECT OF AQUEOUS PEEL EXTRACT OF *Musa sapientum* ON SOME LIPID PROFILE OF HYPERLIPIDEMIC RATS

Groups (n=5)	Serum Tc (mg/dl)	Serum TAG (mg/dl)	Serum HDL-c (mg/dl)	Serum LDL-c (mg/dl)
NC	84.50 ± 9.19 ^{a}	53.17 ± 14.00 ^{a}	35.10 ± 5.52 ^{ab}	39.65 ± 11.38 ^{a}
HC	446.53±27.57 ^{d}	743.45 ± 18.77 ^{d}	25.93 ± 4.39 ^{a}	214.5 ± 10.61 ^{d}
H+OMN$_{100}$	247.00±13.00 ^{bc}	273.44±18.90 ^{c}	33.79±11.91^{ab}	158.35±14.04^{c}
H+ORT$_{100}$	134.35 ± 19.86^{a}	202.00 ± 8.48^{b}	33.43 ± 4.85 ^{ab}	72.00 ± 21.21^{b}
H+SRO$_{100}$	277.44 ± 15.01^{c}	289.70 ± 18.87^{c}	35.10 ± 6.00 ^{ab}	178.00 ± 11.31^{c}
H+Std$_{70}$	156.00 ± 16.70^{ab}	220.60 ± 12.50^{b}	46.60 ± 7.50^{b}	89.00 ± 12.83 ^{b}

Values are means of five determination ± SD

Values with different superscripts down the column are statistically different (P<0.05). **NC**: Normolipidemic control; **HC**: Hyperlipidemic Control; **H+SRO$_{100}$**: Hyperlipidemic rats + Saro Extract (100mg/kg); **H+ORT$_{100}$**: Hyperlipidemic rats + Oranta Extract (100mg/kg); **H+OMN$_{100}$**: Hyperlipidemic rats + Ominni Extract (100mg/kg); **H+Std$_{70}$**: Hyperlpidemic rats + Standard drug (Atorvastatin) (70mg/kg). **Tc**: Total cholesterol; **TAG:** Triacylglycerol; **HDL-c**: High density lipoprotein cholesterol; **LDL-c:** Low density Lipoprotein cholesterol.

Table 2: EFFECT OF AQUEOUS PEEL EXTRACT OF *Musa sapientum* ON SOME LIPID PROFILE OF NORMOLIPIDEMIC RATS

Groups (n=5)	Serum Tc (mg/dl)	Serum TAG (mg/dl)	Serum HDL-c (mg/dl)	Serum LDL-c (mg/dl)
NC	84.50 ± 9.01 [a]	53.17 ± 14.00 [a]	35.10 ± 5.52 [a]	39.65 ± 11.38 [a]
N+OMN$_{100}$	86.67 ± 15.19 [a]	61.42 ± 12.50 [a]	33.80 ± 4.50 [a]	31.85 ± 7.28 [a]
N+ORT$_{100}$	64.43 ± 9.81 [a]	41.00 ± 6.93 [a]	39.07 ± 7.70 [a]	17.13 ± 3.59 [a]
N+SRO$_{100}$	104.00 ± 16.87 [a]	57.40 ± 18.80 [a]	36.40 ± 4.50 [a]	80.50 ± 14.85 [b]

Values are means of five determination ± SD

Values with different superscripts down the column are statistically different (P<0.05). **NC:** Normolipidemic control; **N+SRO$_{100}$**: Normal rats + Saro Extract (100mg/kg); **N+ORT$_{100}$**: Normal rats + Oranta Extract (100mg/kg); **N+OMN$_{100}$:** Normal rats + Ominni Extract (100mg/kg); **Tc:** Total cholesterol; **TAG:** Triacylglycerol; **HDL-c:** High density lipoprotein cholesterol; **LDL-c**: Low density Lipoprotein cholesterol.

Discussion

A single injection of poloxamer-407 has been shown to cause elevations of serum cholesterol and triglyceride levels in rats [8]. In the present study, the rats treated with P-407 were characterized by high serum lipid profiles. P-407 is a block copolymer composed of a hydrophobe that is flanked on each side by hydrophilic polyoxyethylene units [15]. A rapid, convenient and low-cost hyperlipidemic animal model had been developed based on the administration of P-407 [8]. P-407-induced hyperlipidemia is associated with alterations in activity of 3-hydroxy-3- methylglutaryl-CoA (HMG-CoA) reductase, lipoprotein lipase (LPL), lecithin cholesterol acyltransferase (LCAT), cholesteryl ester transfer protein (CETP), hepatic lipase (HL) and lipoprotein lipase (LPL) P-407 directly inhibits the heparin releasable fraction of LPL and HL, and it indirectly increases the biologic activity of CETP and LCAT [16].

Hyperlipidemia progresses with alteration in the serum lipids profile. Therefore, the lipids profile: Tc, TAG, LDL-c and HDL-c are important risk factors in many degenerative diseases [5]. There was a significant increase ($p<0.05$) in the level of Tc, TAG, and LDL-c in the untreated hyperlipidemic group as compared with hyperlipidemic extract treated, Atorvastatin treated and normal control groups. This effect is of significant value since serum lipids profile is an important risk factor to many diseases like cardiovascular diseases, hypertension, etc [6]. The comparison of aqueous peel extracts of Ominni, Saro and Oranta, showed a better lipid lowering potential in the Oranta peel extract.

The hypocholesterolemic activity of the peel extracts may be due to a number of mechanisms; inhibition of HMG-CoA reductase, stimulation of Cholesterol-7-alpha-hydroxylase, which converts cholesterol into bile acids, or inhibition of cholesterol absorption from the intestine due to formation of complexes with compounds such as glycosides and saponins [17]. A reduction in Triacylglycerol level may be due to decreased lipogenesis, increased lipolytic activity by inhibition of hormone-sensitive lipase or the lipogenic enzymes [18], or activation of lipoprotein lipase as have been proposed for some antihyperlipidemic plants [19,20].

The peels extract lipid lowering effect is comparable to that of Atorvastatin. However, there was no significant ($p<0.05$) difference in the serum HDL-c of the peel extracts when compared to the normal group. These could mean that the peel extracts may not have boosting ability to HDL-c while the animals in group treated with Atorvastatin shows a significant ($p<0.05$) higher value in HDL-c when compared to other groups. HDL-c carries cholesterol and cholesterol esters from the peripheral tissues and cells to the liver, where cholesterol is metabolized into bile acids. This pathway plays a very important role in reducing cholesterol levels in the blood and peripheral tissues and in inhibiting atherosclerotic plaque formation in the aorta [21,22].

Atorvastatin is used for the treatment of elevated total cholesterol, LDL, triglycerides and to elevate HDL-c. It prevents the production of cholesterol in the liver by blocking HMG-CoA reductase [13].

Hyperlipidemia is a major risk factor for the development and progression of atherosclerosis and coronary artery disease [23,24]. In hyperlipidemia, there is an increase in serum Tc TAG and LDL-c levels, which results in an increased risk for the development of atherosclerosis. Thus, regulating serum cholesterols level is important for atherosclerosis prevention, as it has been shown that atherosclerosis can be suppressed by controlling the levels of serum cholesterol. The therapeutic benefits of plant extracts that are without side effects have been the focus of many recent extensive studies [25].

Most cholesterol in the body is present as an essential component of the cell membrane, while the remainder is in transit through the blood or functions as a starting material for the biosynthesis of bile acid, steroid hormones, and vitamin-D [8]. Elevated levels of serum TAG and LDL-c that are accompanied by reduced HDL-C levels are often associated with an increased risk of coronary heart disease [26]. In the hyperlipidemic groups, the highest ($p<0.05$) reduction in the lipid profile was made by Oranta cultivar suggesting it as the best candidate among other cultivars for the treatment of hyperlipidemia and other cardiovascular related diseases.

The normal rats treated with the peel extracts shows no significant difference in the lipid profile compare to normal control group except the LDL-c of animals treated with Saro which was significantly ($p<0.05$) increased. According to many studies, LDL-c is considered the most dangerous among the serum lipids, and the oxidation of LDL-c leads to its increased penetration of arterial walls [23]. Moreover, elevated LDL-c levels play a crucial role in the development of atherosclerotic lesions that progress from fatty streaks to ulcerated plaques [27]. Thus, serum LDL-c levels are used as the basis for initiating and monitoring the treatment of patients with elevated blood cholesterol levels [28,29].

Conclusion and recommendation:

The present comparative study evaluated the hypolipidemic effects of aqueous peel extracts of three cultivars of *Musa sapientum* on the lipid profile of poloxamer-407 induced hyperlipidemic rats. It was observed that rats treated with Oranta peel extract had lipid lowering activity similar to the standard drug (atorvastatin) when compared to Ominni and Saro peel extracts. The results from this research revealed that the *M. sapientum* peel extract has antihyperlipidemic properties and reduces the risk of cardiovascular diseases. Thus intake of peel extracts of *M. sapientum*, particular the Oranta cultivar as drug might have potential benefit in the management and/or treatment of hyperlipidemia. At present the exact mechanism of action of *M. sapientum* is not fully known hence, further investigations in this direction are needed for possible isolation and structural elucidation of the antihyperlipidemic component *M. sapientum.* This might help to establish definitive evidence for the implication of *M. sapientum* extract on rat cholesterol metabolism.

Conflict of interest statement:

Authors have declared that no competing interests exist.

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Authors' contribution:

CE performed this study, DBJ and OAO performed the statistic analyses, DBJ and SIRO designed the study. The article was written by CE but the present version was written by SIRO. All authors read and approved the final manuscript.

REFERENCE

[1] V.M. Montori, J.P. Brito, H.H. Ting: Patient-centered and practical application of new high cholesterol guidelines to prevent cardiovascular disease. Journal of America Medical Association 2014; 311:465–466.

[2] C. Huang, C. Cen, C.X. Wang, H. Zhan and X. Ding: Synergistic effects of colchicine combined with atorvastatin in rats with hyperlipidemia. Lipids in Health and Disease 2014; 13:67.

[3] R. Chattopadhyaya, D. Pathak and D.P. Jindal. In: Hypolipidemic activity of Nathaichoori Chooranam (NC) (Siddha drug) on High fat diet Induced Hyperlipidemic Rats. Ed: Kanakavalli K, Thillaivanan S and Parthiban P. International Journal of Pharmaceutical Research Science 2014; 02(1):104-109.

[4] R.H. Raasch: Hyperlipidemias. In: Applied Therapeutics. The Clinical Use of Drugs edited by Young LY and Koda-Kimble MA (Edwards Brothers, Ann Arbor, MI) 1988; 9: 1743

[5] O.A. Sodipo, F. Abdulrahman and U. Sandabe: Effects of the Aqueous Fruit Extract of Solanum macrocarpum Linn. on Hematological Parameters of Chronic Triton-Induced Hyperlipidemic Rats. Journal Phys Pharm Adv. 2012; 2(2): 122-132.

[6] O.T. Kolawole, S.O. Kolawole, A.A. Ayankunl and I.O. Olaniran: Methanol Leaf Extract of Persea Americana Protects Rats against Cholesterol-Induced Hyperlipidemia. British Journal of Medicine & Medical Research 2012; 2(2): 235-242.

[7] N. Nazmun-Naher, K. Alam, S. Islam, A.K.M. Al-Mamun, M. Hossain, A.A. Rahman and M. Rashid: Effects of Acacia nilotica Leaf Extract on Adrenaline-induced Hyperlipidemia and Cardiac Remodeling in Rats. Bangladesh Pharmaceutical Journal 2012; 15(2): 135-139.

[8] S.Y. Hor, E. Farsi, M.F. Yam, N.M. Nuyah and M.Z. Asmawi: Lipid-lowering effects of Coriolus versicolor extract in poloxamer 407-induced hypercholesterolaemic rats and high cholesterol-fed rats. Journal of Medicinal Plants Research 2011; 5(11):2261-2266

[9] C.H.C. Chakraborty, C.H. Hsu, Z.H. Wen, C.S. Lin, G. Agoramoorthy: Zebrafish: a complete animal model for in-vivo drug discovery and development. Current drug metabolism 2009; 10(2):116-124
[10] R. Baskar, S. Shrisakthi, B. Sathyapriya, R. Shyammpriya, R. Nithya, P. Pongodi: Antoxidant Potential of Peel Extracts of Banana Varieties (Musa sapientum). Food and Nutrition Science 2011; (2):1128-1133
[11] E. De-Langhe, E. Hribova, C. Sebastien, D. Jaroslav and S. Rony: Did backcrossing contribute to the origin of hybrid edible bananas? Annals of botany 2010; 106(6):849-857
[12] D. Lorke: A new approach to practical acute toxicity testing. Archive Toxicology 1983; 54:275-287.
[13] M. Abdulazeez: Effect of Peristrophe bicalyculata on lipid profile of P- 407-induced hyperlipidemic Wistar rats. Journal of Medicinal Plants Research. 2011; 5(4): 490-494.
[14] E.A. Stein: Lipids, lipoproteins and apolipoproteins. In: Tietz NW (ed) Fundamentals of Clinical Chemistry. WB Saunders, Philadelphia. 3rd Edition, 1987: 470-479.
[15] T.P. Johnston, W.K. Palmer: Mechanism of poloxamer 407-induced hypertriglyceridemia in the rat. Biochemical Pharmacology 1993; 46: 1037-1042.
[16] O.S. Olorunnisola, G. Bradley and A.J. Afolayan: Protective Effect of T. violacea Rhizome Extract Against Hypercholesterolemia-Induced Oxidative Stress in Wistar Rats. Molecules 2012; 17: 6033-6045
[17] D.B. James, N. Elebo, A.M. Sanusi and L. Odoemene: Some Biochemical Effect of Intraperitoneal Administration of Phyllanthus amarus Aquoeus Extacts on Normaglycemic Albino Rats. Asian Journal of Medical Sciences 2010; 2(1):7-10
[18] L. Pari, and S. Venkateswaran: Protective role of Phaseolus vulgaris on changes in the fatty acid composition in experimental diabetes. Journal of Medicinal Food 2004; 7: 204-209
[19] I. Ahmed, M.S. Lakhani, M. Gillett, A. John and H. Raza: Hypotriglyceridemic and hypocholesterolemic effect of anti-diabetic Momordica charantia fruit extract in STZ-induced diabetic rats. Diabetes Research and Clinical Practice 2001; 51: 155-161.
[20] C. Roh and U. Jung: Screening of Crude Plant Extracts with Anti-Obesity Activity. International Journal of Molecular Sciences 2012; 13:1710-1719
[21] H. Kim, D. Jeong, H. Jung, T. Yokozawa, J. Choi J: Hypolipidemic Effects of Sophora flavescens and Its Constituents in Poloxamer 407-Induced Hyperlipidemic and Cholesterol-Fed Rats. Biol. Pharm. Bull 2008; 31(1):73-78.
[22] K. E. Imafidon. Tissue Lipid Profile of Rats Administered Aqueous Extract of Hibiscus Rosa-Sinensis. Linn. Journal of Basic and Applied Sciences 2010; 6(1):1-3.
[23] K. Prasad, J. Kalra: Oxygen free radicals and hypercholesterolemic atherosclerosis: effect of vitamin E. American Heart Journal 1993; 125: 958-973
[24] P.R. Deepa, P. Varalakshmi: Atheroprotective effect of exogenous heparin-derivative treatment on the aortic disturbances and lipoprotein oxidation in hypercholesterolemic diet fed rats. Clin. Chim. Acta, 2005; 355: 119-130.
[25] T. Yokozawa, A. Ishida, E.J. Cho, T. Nakagawa: The effects of Coptidis Rhizoma extract on a hypercholesterolemic animal model. Phytomedicine 2003; 10:17-22.
[26] V. Dhulasavant, S. Shinde, M. Pawar, N.S. Naikwad: Antihyperlipidemic Activity of Cinnamomum tamala Nees. On High Cholesterol Diet Induced Hyperlipidemia. International Journal of PharmTech Research 2010, 2(4): 2517-2521.
[27] O.A. Owolabi, D.B. James, A.B. Ibrahim, O.F. Folorunsho, I. Bwalla and F. Akanta: Changes in Lipid Profile of Aqueous and Ethanolic Extract of Blighia sapida in Rats. Asian Journal of Medical Sciences 2010; 2(4): 177-180.
[28] T. Wu, J. Fu, Y. Yang, L. Zhang, J. Han: The effects of phytosterols/stanols on blood lipid profiles: a systematic review with meta-analysis. Asia Pacific Journal of Clinical Nutrition 2009, 18 (2):179-186
[29] R.O. Arise, A.A. Akintola, J.B. Olarinoye JB and E.A. Balogun: Effects of aqueous extract of Naulea latifolia stem on lipip profile and some enzymes of rat liver and kidney. International journal of pharmacology 2012; 1811-7775