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OUTLOOK ON ANTI-HYPERLIPIDEMIC OUTCOME OF *MORINGA OLEIFERA* IN RELATIONSHIP WITH STATINS

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ABSTRACT

Hyperlipidemia is a metabolic sickness considered by increased concentration of any class of plasma lipids e.g. cholesterol, triglycerides, cholesterol esters or phospholipids. Epidemiological facts have shown that hyperlipidemia is accountable for 4.4 million expiries every year. Statins have been frequently used as anti hyperlipidemic drugs for primary and secondary stages but some natural cures like *Moringa Oleifera* have also been used for treatment of hyperlipidemia. The existing study was directed to link the anti hyperlipidemic effects of Simvastatin and *M.oleifera* in hyperlipidemic patients. It was a cross sectional study in which 30mild to moderate hyperlipidemic male patients in three sets with average age of 35 to 45 years were included. Group I was given placebo (corn starch capsule) while groups II and III were treated with simvastatin (20mg OD) and *M. oleifera* leaf powder capsule (500mg bd) respectively. Blood samples were collected at zero, 15, 30, 45, 60, 75, 90 days. Cholesterol, LDL, HDL and Triglycerides were observed. Statistical analysis was performed using one-way analysis of variance (ANOVA). Results have shown that *M.oleifera* had significantly decreased the value of Cholesterol, LDL and Triglyceride level with a potential result on triglycerides with a value of ($P \leq 0.01$), while there was non-significant difference on HDL by *M.oleifera.* However, Simvastatin

have significantly decreased the level of cholesterol. Study concluded that *M. oleifera* is a better, indigenous and safer therapeutic option. It may suggest to improve the quality of life.

Keywords: Hyperlipidemia, Simvastatin, *Moringa Olifera*, Cholesterol, HDL, LDL

INTRODUCTION

Cardiovascular disease is prominent reason of death among adults; the cause is augmented in people having hyperlipidemia as compare to those having normal cholesterol levels **[1]**. In Bangladesh, Pakistan and India coronary death rates are 50% higher as compared to other populations **[2]**. In Karachi 29.6% adult populations is suffering from CAD **[3, 4]**. According to a study 29.6% population were affected by CAD among 320 selected adult populations in Pakistan **[5]**. Another study indicated that prevalence of CAD among Pakistani population was 3.6% based on physician's diagnosis **[6]**. CAD is reported to kill 3.8 million people in China in 1991 and the mortality rate in China due to CAD is also increased from 1980 to 2000 **[7]** In the United States 62 deaths out of 125, in Finland 38 out of 111, in Poland, 20% of all deaths, and in Netherlands 16 out of 50 deaths occurred due to coronary heart disease. **[8]**. Hyperlipidemia is defined as the marked elevation of any class of plasma lipids or lipoproteins **[9]**. It is categorized in five clinical syndromes according to nature of lipoprotein involve; Type 1: Hyperchylomicronemia, Type 2: Combined Hyperlipoproteinemia Type 3: Hyperlipoproteinemia Type 4: Familial Hypertriglyceridemia Type 5: Mixed Hypertriglyceridemia **[10]**. Among all these type 2 reflected as most prevalent. This type is also responsible for development of atherosclerosis. Moreover hyperlipidemia impairs bone regeneration **[11]** and induces secondary hyperparathyroidism **[12]** Lipoproteins are classified in different types according to their size, density and electrophoretic strength. Major types of lipoproteins are; Low density lipoproteins (LDL), High density lipoproteins (HDL), Very low density lipoproteins (VLDL), Intermediate density lipoproteins (IDL), and chylomicrons. Each class has specific role in proliferation and metabolism of plasma lipids **[13]**. LDL commonly known as bad cholesterol is key element in atherogenic cascade. LDL plays an important role with the focal influx at the arterial sites, it work as a chemotactic factor for the blood monocytes at the site where lesion is already developed. In the case of hyperlipidemia the process of recruitment of macrophages and

atherogenesis exacerbates. Recruited monocytes further go with the chemotactic protein-1 and oxidatively modified LDL to produce a mature atherosclerotic plaque. Reactive oxygen species modify the lipoproteins and these modified lipoproteins are accepted by macrophages scavenger receptors. After up taking they are converted into foam cells and theses foam cells are the early step of atherosclerosis **[14]**. Since many years statins are used for treatment of these malicious diseases. Mode of action of statins are by inhibiting rate limiting enzyme HMG-CoA reductase which converts the HMG-CoA to mevalonic acid (a precursor for de novo synthesis of cholesterol) and increasing the LDL receptors which causes the binding of circulating LDL and decreasing the concentration of LDL in plasma **[15]**. Additionally statins also exhibit anti-inflammatory property, suppress T cells activation, macrophage infiltration; reduce plaque formation and atherosclerosis **[16]**. They also exert some beneficial effects on atrial fibrillation, post coronary bypass grafting and short term treatment of heart failure **[17]**. Among statins simvastatin is a commonly used drug because of its lipophilic nature **[18]**. It not only cause reduction in LDL and VLDL level but also cause a positive increase in HDL level in hyperlipidemic patients having LDL cholesterol ≥160 mg/dl (4.2 mmol/L) and triglycerides ≤400 mg/dl (4.5 mmol/L) **[16, 18]**. One most important effect of Simvastatin is the release of Vascular Endothelial Growth Factor (VEGF) by vascular smooth muscle cells. This factor is necessary in repairing of atherosclerotic induced endothelial damage and due to this reason Simvastatin is a preferred agent among statins since years **[19]**. Animal studies have shown that leaves of *M.oleifera* can increase the fecal cholesterol and decrease plasma cholesterol **[20].** Leaves, roots and flowers of *M. Oleifera* are reported for highly antioxidant properties and are best anti-hyperlipidemic and antioxidant therapy **[21]**.

MATERIAL METHODS

Study design, It was a cross sectional comparative study, was conducted in the Johar Institute of Professional Studies-School of Pharmaceutical Sciences (JIPS-SPS), Lahore, Punjab, Pakistan and was approved by the Ethics Committee and Human Studies Review Board of the institute.

Selection criteria individuals have mild to moderate hyperlipidemia, having 200-250mg/dl of total cholesterol level and not taking medicines for other health conditions were included. Subjects were excluded if

they had a BMI greater than 35 kg/m2, high total cholesterol value usually >280mg/dl, history of Autoimmune and Neurological diseases, hypersensitive to Simvastatin and those who have history of allergy to statins and *Moringa oleifera.*

Group Distribution A total of 30 male individuals having moderate hyperlipidemia (200-250mg/dl of total cholesterol level), were selected for the study and were divided randomly into three groups as shown in Table 1. Subjects were instructed not to change their normal daily routine including medications, foods, and exercise activities.

Collection of blood samples Blood samples were taken in sterilized glass tubes as per schedule shown in Table 2. After taking the blood samples glass tubes were carefully placed in centrifuge and for 15 minutes at 4000 rpm all the samples were centrifuged. After centrifugation serum was separated and stored in the small eppendorfs. Eppendorfs were stored at -20°C until they were used for further analysis.

Table 1: Groups Distribution

Total number of groups	Chemicals	Dosing
Group I	Corn starch	500mg twice daily
Group II	Simvastatin	20mg once daily
Group III	*M.oleifera* leaf powder	500mg twice daily

Table 2: Blood sampling schedule

Total number of collections	Days	Amount of blood taken from each individual
1st collection	Zero	5ml
2nd collection	15	5ml
3rd collection	30	5ml
4th collection	45	5ml
5th collection	60	5ml
6th collection	75	5ml
7th collection	90	5ml

Evaluation of Lipid Biomarkers Lipid profile parameters including total cholesterol, low density lipoproteins cholesterol, high density lipoprotein cholesterol and triglycerides were determined after analysis of serum samples with the help of lipid profile kits through chemistry analyzer.

Statistical Analysis Data were analyzed by Mean+/- Standard deviation. Analysis of variance ANOVA test were applied in which probability value of </0.05 were considered as significant

RESULTS

The results showed in Fig-1 that in Group 1 (Placebo treated) the serum cholesterol level was significantly reduced ($P \leq 0.01$) at day 15 (225±9.34) and ($P \leq 0.05$) day 75 (235.50±14.05), respectively when compared with the serum cholesterol level at day 0 (272.20±13.04). Fig-2sowed Group 2

(Simvastatin Treated), serum cholesterol level was significantly reduced (P ≤ 0.05) at day 75 (183.00±10.94) and day 90 (176.30±14.03), respectively when compared with the serum cholesterol level at day 0 (229.60±15.52). Fig-3 reflected that in Group 3 (*M. oleifera* Treated*)*, the serum cholesterol level was significantly reduced (P ≤ 0.001) at day 75 (183.10±11.63) and day 90 (162.00±9.11), respectively when compared with the serum cholesterol level at day 0 (201.90±9.59).

Fig-4 in Group 1 (Placebo Treated) the serum LDL level was significantly increased (P ≤ 0.05) at day 60 (166.50 ± 3.06), day 75 (165.70 ± 9.20) and day 90 (165.70 ± 8.54) respectively when compared with the serum LDL at day 0 (136.20 ± 10.20) Fig-5 in Group 2 (Simvastatin Treated) there was non-significant difference in the serum LDL level from day 0 (127.50 ± 17.91) to day 90 (109.70 ± 16.03) although mild increase in LDL was seen at day 30 (154.30 ± 11.29) and day 60 (151.80 ± 7.73) respectively which was non-significant difference.Fig-6 in Groups 3 *(M.oleifera,* Treated) the serum LDL was significantly reduced (P ≤ 0.05) at day 90 (92.70 ±8.66) when compared with serum LDL at day 0 (162.50 ± 22.25).

Fig-7 in Group 1 (Placebo Treated) the serum HDL was significantly increased (P ≤ 0.01**)** at day 90 (55.20± 4.51) when compared with the serum HDL level at day 0 (40.70± 2.47).Fig-8 in Group 2 (Simvastatin Treated) there was non-significant difference in the serum HDL level from day 0 (43.60 ± 2.85) to day 90 (39.30 ± 1.43) although mild increase in LDL was seen at day 60 (46.60 ± 1.43) which was non-significant difference.Fig-9 in Group 3 (*M. oleifera* Treated) there was non-significant difference in the serum HDL level from day 0 (34.50 ± 1.77) to day 90 (38.70 ± 1.82).

Fig-10 in Group 1 (Placebo Treated) there was non-significant difference in the serum Triglyceride level from day 0 (157.80 ± 7.72) to day 90 (161.60 ± 7.79). Fig-11 in Group 2 (Simvastatin Treated) there was non-significant difference in the serum Triglyceride level from day 0 (169.40 ± 151.81) to day 90 (148.30 ± 11.11). Fig-12 in Group 3 *(M.oleifera* Treated) the serum triglyceride level was significantly reduced (P ≤ 0.01) at day 75 (118.70 ± 8.78) and at day 90 (117.50 ± 8.78) respectively when compared the serum Triglyceride level at day 0 (202.17 ± 22.17).

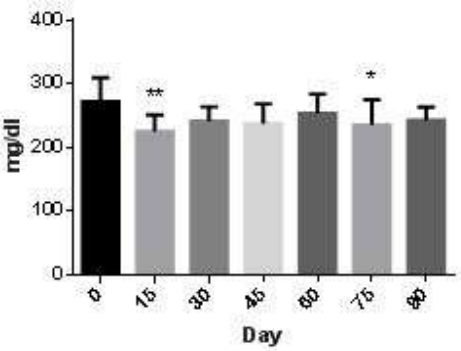

Fig-1 Serum cholesterol level of group 1

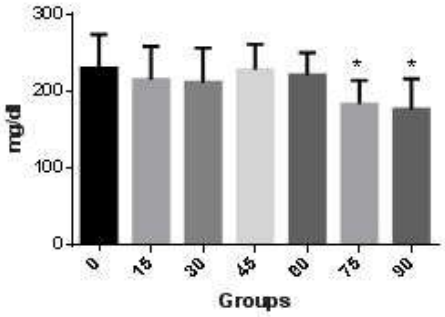

Fig-2 Serum cholesterol level of group 2

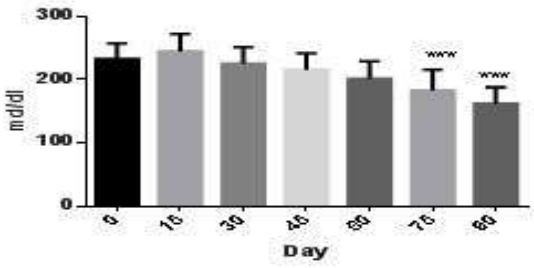

Fig-3 Serum cholesterol level of group 3

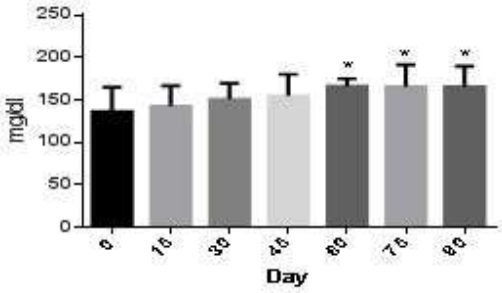

Fig-4 Serum LDL level of group 1

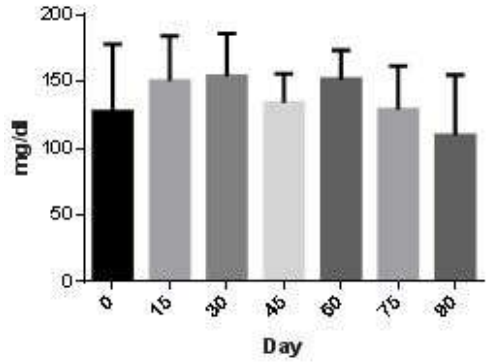

Fig-5 Serum LDL level of group 2

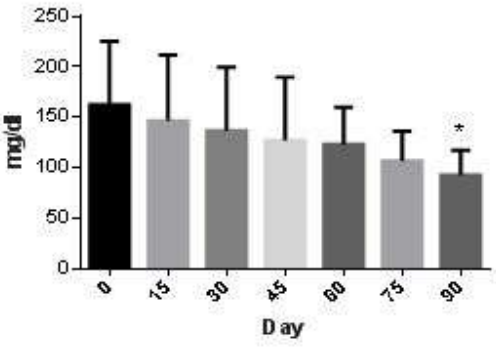

Fig-6 Serum LDL level of group 3

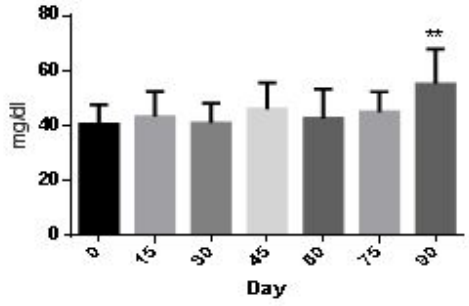

Fig-7 Serum HDL level of group 1

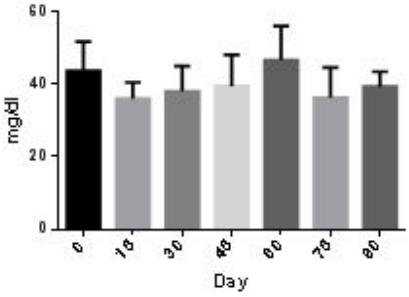

Fig-8 Serum HDL level of group 2

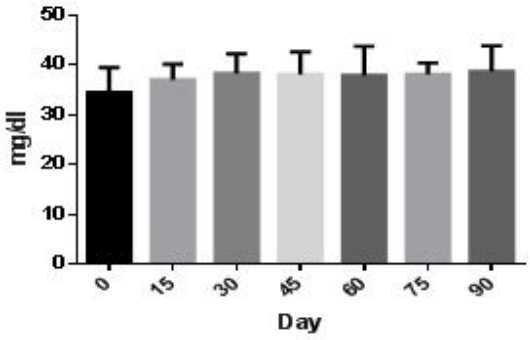

Fig-9 Serum HDL level of group 3

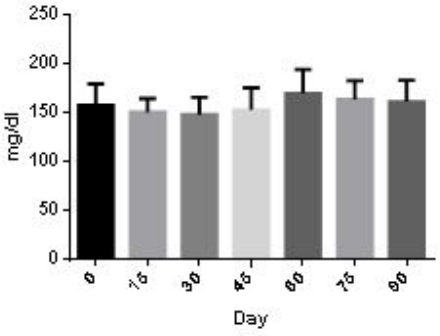

Fig-10 Serum Triglyceride level of group 1

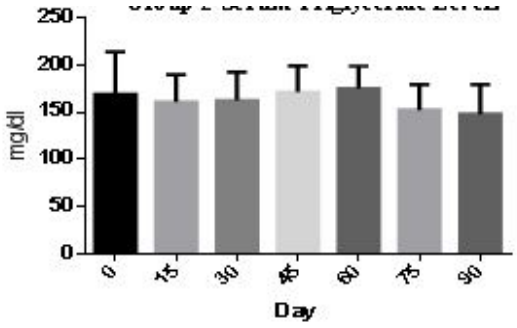

Fig-11 Serum Triglyceride level of group 2

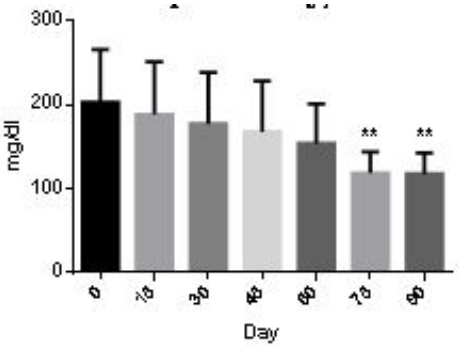

Fig-12 Serum Triglyceride level of group3

DISCUSSION

The current reading surveyed the hypolipidemic effect of *Moringa oleifera* in human beings, Moringa leaves has been reported as lipid lowering agents and normalizing property on blood pressure, the findings of current study is discussed below **[22, 23].**

Lipids are small molecules which are not soluble in water are transported in the blood

in the protein capsule so that they are termed as lipoproteins and their sizes determines the type of lipoprotein mainly divided into two types HDL (High density lipoprotein) and LDL (Low density Lipoprotein). Abnormalities of these lipoproteins and triglycerides are now common which are influential factors of atherosclerosis and these abnormalities ultimately leads cardio vascular disease (CVD) and Coronary heart disease (CHD) **[24]**.The present study showed that cholesterol level was decreased in group 2 at day 75 and 90, which confirms the already reported anti-hyperlipidimic effect of simvastatin but the results were highly significant in group 3 (Moringa treated), as substantial decrease was observed at day 75 and 90 in serum cholesterol level, which reflect the potent anti-hyperlipidimic activity of Moringa powder. These results are in concordance with the previous studies of Rauchand its colleagues **[25]**.

Serum LDL level showed significant fall at day 90 in moringa treated (group 3), but there were no marked decrease in both group 1 and 2. Which classify the moringa powder, as LDL lowering agent. These results are same as previous been reported by Ghasi and its colleagues **[26]**

Serum HDL levels were not much affected by moringa treated group however, significant elevation was observed at day 90 in simvastatin treatment group. This property of Simvastatin make him drug of choice for treatment of hyperlipidemia **[27, 28].**

Moringa treated group show substantialdecrease in serum triglycerides level at day 75 and 90, these changes were more potent among all changes in lipid markers during this study, while simvastatin treated group also show decrease in triglycerides level but the change were not up to the mark as compare to moringa treated group **[29, 30]**.

CONCLUSION

Leaf powder of Moringa oleiferain dose of 500mg capsule twice a day is an effective lipid lowering agent and there is potent effect on serum triglycerides as compare to simvastatin. It is a better, indigenous, less expansive and much safe therapeutic option .It may be suggested to improve the quality of life and to overcome the side effect profile of allopathic anti-hyperlipidemic therapies.

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CONFLICT OF INTERESTS

Authors declare no conflict of interests.

REFERENCES

[1] Mozaffarian D, Benjamin EJ, Go AS. 2016. Heart disease and stroke statistics, update: a report from the American Heart Association. Circulation. 133(4), 338-60.

[2] Mckeigue MP. 1992. Coronary heart disease in Indians, Pakistanis, and Bangladeshis: aetiology and possibilities for prevention.Br Heart .J. 67(5), 341–42.

[3] Bhalli MA, Kayani AM, Samore NA. 2011. Frequency of Risk Factors in Male Patients with Acute Coronary Syndrom. J. Physician and Surgeons Pakistan.21, 271-75.

[4] Harikumar K, Abdul-Althaf S, Kumar BK, Ramunaik M, Suvarna CH. 2013. A Review on Hyperlipidemia. J. Novael Trends in Pharmaceutical Sciences**4**, 2277-82.

[5] Jafar TH, Jafary FH, Jessani S, Chaturvedi N. 2005. Heart disease epidemic in Pakistan: women and men at equal risk. American heart journal, 150(2), 221-26.

[6] Jafar TH, Qadri Z, Chaturvedi N. 2007. Coronary artery disease epidemic in Pakistan-more electrocardiographic evidence of ischemia in women than in men.

[7] Keys A. 1970. Coronary heart disease in seven countries.circulation41, 186-95.

[8] Gofman JW, Young W. Tandy R. 1966. Ischemic heart disease, atherosclerosis and longevity. Circulation.34, 679-97.

[9] Fredrickson DS, Levy RI, Lees RS. 1967. Fat transport in lipoproteins-an integrated approach to mechanisms and disorders. New Eng. J. Med.276, 34-44.

[10] Stanley P, Chartrand C. Davignon A. 1965. Acquired aortic stenosis in a twelve year old girl with xanthomatosis: successful surgical correction. New Eng. J. Med.273, 1378-80.

[11] Parhami F, Tintut Y, Beamer WG, Gharavi N, Goodman W. Demer LL. 2001. Atherogenic high-fat diet reduces bone mineralization in mice. J. Bone Miner Res.16, 182-88.

[12] Sage AP, Lu J, Atti E, Tetradis S, Ascenzi MG, Adams DJ, Demer LL, Tintu, Y. 2011. Hyperlipidemia induces resistance to PTH bone anabolism in mice via

oxidized lipids. J. Bone Miner Res. 26(6), 1197-206.

[13] Rall SC, Weisgraber KH, Mahley RW, Ogawa Y, Fielding CJ, Utermann G, Assmann G. 1984. Abnormal lecithin: cholesterol acyltransferase activation by a human apolipoprotein AI variant in which a single lysine residue is deleted. Journal of Biological Chemistry. 259(16), 10063-70.

[14] Sage, AP, Lu J, Atti E, Tetradis S, Ascenzi MG, Adams DJ, Demer LL, Tintut Y. 2011. Hyperlipidemia induces resistance to PTH bone anabolism in mice via oxidized lipids. J. Bone Miner Res. 26(6), 1197-206.

[15] Tobert JA. 1987. New developments in lipid-lowering therapy: the role of inhibitors of hydroxymethylglutaryl-coenzyme A reductase. Circulation.76 (3), 534-8.

[16] Antonopoulos AS, Margaritis M, Lee R, Channon K. Antoniades C. 2012. Statins as anti-inflammatory agents in atherogenesis: molecular mechanisms and lessons from the recent clinical trials. Curr Pharm Des.18, 1519-30.

[17] Amarenco P, Goldstein LB. Szarek, M. 2007. Effects of intense low-density lipoprotein cholesterol reduction in patients with stroke or transient ischemic attack. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial 38(12), 3198–220

[18] Marot A, Morelle J, Chouinard V. A, Jadoul M, Lambert M. Demoulin N. 2011. Concomitant use of simvastatin and amiodarone resulting in severe rhabdomyolysis: a case report and review of the literature. ActaClin Belg. 66(2), 134-36.

[19] Jones P, Kafonek S, Laurora I,Hunninghake D. 1998. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia (the CURVES study). The American journal of cardiology.5, 582-87.

[20] Mehta K, Balaraman R, Amin AH, Bafna PA, Gulati OD. 2003. Effect of fruits of *Moringa oleifera* on the lipid profile of normal and hypercholesterolaemic

rabbits. J. Ethnopharmacol. 86, 191–95.

[21] Chumark P, Khunawat P, Sanvarinda Y, Phornchirasilp S, Morales NP, Phivthong-Ngam L, Ratanachamnong P, Srisawat S, Pongrapeeporn KU. 2008. The in vitro and ex vivo antioxidant properties, hypolipidaemic and antiatherosclerotic activities of water extract of *Moringa oleifera* Lam. leaves. J. Ethnopharmacol. 116, 439–46.

[22] Wang TY, Newby LK, Chen AY, MulgundJ, Roe MT, Sonel AF, Bhatt DL, DeLong ER, Ohman EM, Gibler WB, Peterson ED. 2009. "Hypercholesterolemia paradox in relation to mortality in acute coronary syndrome". Clinical Cardiology. 32(9), 22–8.

[23] Dahot R. 1998. "Vitamin contents of flowers and seeds of Moringa Oleifera" Pakistan Journal of Biochemistry. 21, 1-24

[24] Barter, P, Gotto AM, LaRosa JC, Maroni J, Szarek M, Grundy SM, Fruchart JC. 2007. HDL cholesterol, very low levels of LDL cholesterol, and cardiovascular events. New England Journal of Medicine, 357(13), 1301-10.

[25] Rauch U, Osende JI, Chesebro JH, Fuster V, Vorchheimer DA, Harris K, Badimon JJ. 2000. Statins and cardiovascular diseases: the multiple effects of lipid-lowering therapy by statins. Atherosclerosis. 153(1), 181-89.

[26] Ghasi, S, Nwobodo E, Ofili JO. 2000. Hypocholestrolemic effects of crude extract of leaf of *Moringa oleifera* Lam in high-fat diet fed Wistar rats. J. Ethnopharmacology. 69, 21–5.

[27] Dangi SY, Jolly CI, Narayana S. 2002. Antihypertensive activity of the total alkaloids from the leaves of Moringa oleifera. Pharm Biol.40, 144-48.

[28] Pratik KC, Vinodini NA, Ranjith S, Rakshatha R, Anwar A. 2013. Effect of Moringa oleifera leaf extract on cadmium induced renal toxicity in adult Wistar Albino rats International Journal of Advanced Research 1(5), 162-65.

[29] Nikkon F, Saud A, Haque ME, Aragianis K, Mosaddik MA. 2003. Isolation of Aglycone of

DeoxyNiazimicin from Moringa oleifera Moringa oleifera Lam. and cytotoxicity, Rev. Latinoamer. Quim. 31(1), 5-9.

[30] Lewis GF, Rader DJ. 2005. "New insights into the regulation of HDL metabolism and reverse cholesterol transport". Circulation Research. 96(12), 1221–32.