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ANTIHYPERLIPIDEMIC EFFECT OF MIMUSOPS LARIFOLIA BUTANOLIC EXTRACT ON HIGH-FAT DIET-INDUCED OBESE RAT

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ABSTRACT

Medicinal plants have been used since immemorial time to treat and prevent human ailments. *Mimusops Larifolia* is a medium sized evergreen tree belonging to family Sapotaceae which is widely used in the treatment of different ailments in traditional system of medicine in ancient Egypt. *Mimusops Larifolia* species was recorded to have several pharmacological activities like antimicrobial, antioxidant, anti-inflammatory, hypotensive, antihyperlipidemic, antitumor as it possess a number of phytochemical constituents which have been identified in this plant. Obesity is a significant risk factor associated with many complications such as cardiovascular diseases, diabetes, osteoarthritis, liver and kidney diseases, pancreatitis, cancer and chronic diseases. Obesity is a chronic disease that develops excessive fat accumulation and increase in body weight and result in increased plasma triglycerides, high LDL cholesterol, low HDL cholesterol, elevated blood glucose level and high blood pressure. High Fat Diet (HFD) supplementation have been used in animal models to induce a significant increase in: serum cholesterol, triacylglycerol, , low density lipoprotein(LDL), lipoprotein a (Lip. A), and increase activity of lipase enzymes On contrast, it exhibited a significant decrease in serum levels of High density lipoprotein (HDL). *Mimusops laurifolia* Leaves butanolic extract is selected for our investigation against high fat diet- induced hyperlipidemia in rats as it was able to ameliorate stress induced by high fat diet and showed pronounced curative effect aganist hyperlipidemia and deviated serum atherogenic indices towards control levels. The results of the present study suggest that *Mimusops laurifolia* Leaves extract has the potential to exert curative effect against hyperlipidemia.

Keywords: *Mimusops Larifolia*, High Fat Diet, Hyperlipidemia, Lipase.

1.0 Introduction

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems. **(Khan et al., 2012)**. Although obesity itself appears to augment the incidence of cardiovascular events, it is also associated with major risk factors for atherosclerosis including hyperlipidemia, diabetes mellitus, hypertension, and the metabolic syndrome **(Grundy, 2002)**. Previous researches have shown that hypercholesterolemia, low serum high-density lipoprotein cholesterol (HDL-c) levels and elevated serum low-density lipoprotein cholesterol (LDL-c) levels are prerequisites for atherogenesis **(Alberti et al., 2006)**. Moreover, people with elevated LDL-c levels are at higher risk for CVD **(Soeki et al., 1999)**. Metabolic syndrome refers to a constellation of disturbances including glucose intolerance, central obesity, dyslipidemia (hypertriglyceridemia, elevated non esterified fatty acids (NEFAs), and decreased high-density lipoprotein (HDL) cholesterol), and hypertension **(Azevedo et al., 2002)**.

Another changes related to obesity is the development of non-alcoholic steatohepatitis, which appears as a result of the increased circulating FFAs that are released by adipose tissue in response to insulin resistance. The amount of internalized FFA in liver is not regulated; thus, it is proportional to the plasma, in addition it also increases lipogenesis in the body and enhances intracellular accumulation of TG **(Monteiro et al., 2010).**

In recent years, and especially in developing nations, CVD has become the leading cause of death. A primary contributor to CVD is atherosclerosis, with plaque formation caused by accumulation of lipoprotein deposits in the arterial walls. One of the predominant risk factors for atherogenesis is elevated LDL-c levels **(Kastelein et al., 2008)**.

An increase in circulating concentration of Non-esterified fatty acids (NEFA) reflects the inability of the adipose tissue to buffer the excess nutrient intake and is related to the dyslipidemic state that is typical of the metabolic syndrome. When overload becomes present, the liver increases the production of apo-B containing particles that carry triacylglycerols to the adipose tissue resulting in low-density lipoprotein (LDL) formation **(Laclaustra et al., 2007)**. New risk marker related to lipid metabolism, lipoprotein a (Lip A), have been identified and studied, because its persistently high plasma levels appear to be strong and independently associated with atherosclerosis **(Mota et al., 2008)**.

A positive correlation was observed between Lip A and LDL cholesterol (LDL-c) **(Meabe et al., 2006).** Lip A and total cholesterol (TC) **(Lee et al., 2005)**. and Lip A and apolipoprotein B, which suggests an association between Lip A levels and lipid profile.
According to **(Meabe et al., 2006)**, the fact that high Lip A levels are associated with high LDL-c levels proposes that the LDL metabolism may be involved in the Lip A synthesis. In patients with high LDL-c levels, Lip A is an important factor to determine atherosclerotic disease, as well as its severity and progression rate **(Enas et al., 2006)**.

Cardiovascular disorders are most common cause of mortality world wide **(Epstin, 1992)**. It is well established that hyperlipidemia represents major risk factor for development of atherosclerosis and cardiovascular complications **(Alberti et al., 2006).**
The ideal approach to prevent or to treat atherosclerosis and CVS complications is to target the lipid profile of hyperlipidemic patients using lipid lowering drugs or improving the diet.
Limiting the intake of dietary cholesterol could be an effective approach to prevent Cardiovascular disease **(Liu et al., 2016)**. Elevated LDL-c levels is the predominant risk factors for atherogenesis Which become a primary contributor of CVD the leading cause of death . **(Ghaisas et al., 2008)** investigated antihyperlipidemic activity of methanolic extract of bark of *Mimusops elengi* at 300 and 600 mg/kg in wistar rats and showed significant reduction in levels of triglyceride and total cholesterol as compared to hyperlipidemic group after 7 and 24 hrs of induction whereas HDL level was significantly elevated. It was concluded that *Mimusops elengi* had antihyperlipidemic effect owing to its ability to reduce the levels of total cholesterol, triglyceride and increasing the level of HDL.
(Yu et al., 2011) reported that saponins Significantly reduced the serum total cholesterol and LDL cholesterol in serium . Saponins can be combined with the endogenous cholesterol which is discharged by bile, thus preventing re-absorption of cholesterol and contributing to the emission of cholesterol from the body, reducing the deposition of cholesterol in muscle **(YH and Yu 1990).**

Although *Mimusops elengi* is traditionally being used as cardiotonic and reported for its hypotensive, antiulcer, spasmolytic and antibacterial activity **(Kirtikar et al., 2004).** and is also documented for its presence of flavonoids, steroids, saponins, alkloids, triterpiens, glycosides, **(Rastogi et al., 1999).** There is no phytochemical report available for antihyperlipidemic activity of the species *Mimusops laurifolia*. Hence the present study was designed to investigate the antihyperlipidemic activity of *Mimusops laurifolia* leaves extract on high fat ratio induced hyperlipidemia in rats.

The present study aimed to evaluate the biochemical effects of Leaves extracts of *M. Larifolia* supplementation on hyperlipidemia and Obesity in male rats stressed by high fat diet through some blood parameters .

2.0 Materials and Methods

2.1. Ration and additives :
Animals were fed on ration throughout the acclimatization period of the experiment in the form of pelleted concentrated ration shown in the following table:

1	Carbohydrates	58 %	5	Minerals	1.49 %
2	Protein	20.5 %	6	Calcium	0.98 %
3	Lipid	3.4 %	7	Phosphorus	0.53 %
4	Cellulose	3.1 %	8	Moisture	12 %
Total 100%					

2.2. Plant material :
The Leaves of *Mimusops laurifolia* were collected from the Egyptian museum garden, Cairo, Egypt from July to August 2018.

2.3. Extraction and Fractionation:

2.3..a. Preparation of 80% Methanol Extract :
Hydromethanol (80%) extract was prepared by cold maceration technique. Briefly, 500 g of coarse Leaves powder in a conical flask was mixed with 2.5L of 80%methanol. The flask with its contents was sealed and kept for a period of 48 h at room temperature accompanying intermittent shaking using miniorbital shaker (Bibby Scientific Limited, Stone, Staffordshire, UK) revolving at 120 rpm to enhance the efficient extraction. The entire mixture was first filtered through a funnel plunged with muslin cloth two times and then the filtrate was passed through Whatman filter paper (Number 1) (Maidstone, UK). After filtration, the residue was remacerated two times for a total of 96 h in order to obtain a better yield. The marc was pressed and the combined filtrate was then concentrated using a rotary evaporator (Buchi Model R-200, Switzerland) set at 40 C. The concentrate was pooled together and freezedried using a lyophilizer (Operan, Korea Vacuum Limited, Korea). It rendered a solid residue of yellowish color which was designated as 80% MeOH-E and stored in an air tight container in deep freezer (−20 C) until being used for further investigation.

2.3.b. Fractionation of Crude Extract :
Solvent fractionation of crude extract was carried out using water, chloroform, and n-butanol. Briefly, eighty grams of the crude extract was dissolved in 400mL of distilled water and this solution was transferred to a separating funnel. An equal volume of chloroform was added to it and was shaken vigorously. The mixture was separated in two layers. The chloroform layer (lower) was then removed. The partition with chloroform was repeated two times. All of the chloroform layers were combined and subjected to evaporation using a rotary evaporator (Buchi Model R-200, Switzerland) set at 40 C to get the chloroform fraction, and then the filtrate was placed in an oven at 45 C for one week to remove the remaining solvent. To the separating funnel containing aqueous layer, 400mL of n-butanol was added.
The upper layer in this case was n-butanol, which was separated and the procedure was repeated two times. The separated n-butanol layers were pooled and concentrated using a rotary evaporator (Buchi model R-200, Switzerland) set at 40C to obtain the n-butanol fraction, and then the filtrate was placed in an oven at 45C for two weeks to remove the remaining solvent. The remaining aqueous layer (lower in this case) was concentrated in a lyophilizer (Operan, Korea Vacuum Limited, Korea) to remove water. After drying, the solvent fractions were stored in an air tight container in refrigerator until being used for evaluation of phytochemical constituents **(Molla et al., 2017).**

2.4. Experimental animals :
Sixty (60) male albino rats, 6-8 weeks old, with average body weight 150-200 gm used in the experimental investigation of this study, and purchased from "The Laboratory Animals Research Center", Faculty of Veterinary Medicine, Benha University. Rats were housed in separate wire mesh cages, exposed to good ventilation, humidity and to a 12-hr light/dark cycle, and provided with a constant supply of standard pellet diet (its composition is explained in the table below) and plenty of fresh, clean drinking water ad-libitum.

2.5. Experimental design :
Rats were allocated into six groups of consisting of 10 rats in each, placed in individual cages and classified as following: (Group 1): serves as Normal –control group and provided with standard pellet diet only (Group 2): Receive oral dose of *Mimusops Larifolia* Leaves butanol extract (M.Bu E) at 75.83 mg/kg b.wt. for 8 weeks, (Group 3): Receive oral dose of (M.Bu E) at 151.66 mg/kg b.wt. for 8 weeks, (Group 4): fed on high fat diet daily for 2 months and servcd as HFD stressed group (Group 5): fed on high fat diet daily for 8 weeks; for induction of oxidative stress, besides it receive oral dose of (M.Bu E) at 75.83 mg/kg b.wt. (Group 6): fed on high fat diet daily for 8 weeks; for induction of oxidative stress, besides it receive oral dose of (M.Bu E) at 151.66 mg/kg b.wt .
N.B:
During the experimental period, the dosage was adjusted every week according to any change in body weight to maintain similar dose per kg body weight of rat over the entire period of study for each group.

2.6. Sampling :
At end of the 4th and 8th weeks from onset of experiment period, blood samples were collected from all animals groups (control and experimental groups) . Samples were collected from medial canthus of the eyes of all animal groups and were centrifuged at 3000 rpm for 30 minutes to separate serum. The non hemolyzed carefully separated serum was transferred into clean dry eppendorf tube which kept frozen at -20°C until used for biochemical analysis.

3.0 Result

The obtained data revealed that, administration of *mimusops laurifolia* extract (at a dose of 80 and 160 mg/kg b.wt.) only to normal rat groups (G2 & G3) exhibited non significant decrease in TC, TG concentrations accompanied with non significant increase in serium HDL-C concentration Whereas it exhibited a significant decrease in serium LDL-C, Lip. A cocentrations, and serium Lipase Activity. after 4th and 8th weeks when compared with control normal group .
HFD Supplementation to normal rat group (G4) for 2 months exhibited a significant increase in serium TC, TG, LDL-C, Lip. A concentrations and Lipase Activity. On contrast ،It exhibited a significant decrease in serium HDL-C concentration when compared with control normal group.
The obtained data revealed that, administration of *mimusops laurifolia* extract (at a dose of 80 and 160 mg/kg b.wt.) to HFD-stressed rat groups (G5 & G6) respectivily exhibited a significant decrease in serium TC, TG, LDL-C, Lip. A concentrations accompanied with decrease in serium Lipase Activity. On contrast, It exhibited a significant increase in serium HDL-C concentration after 4th and 8th weeks when compared with none treated HFD-stressed group (G4) .

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Table (1): Effects of Mimusops Larifolia Butanolic Extract treatment on HFD- induced changes in different biochemical parameters

Group	Time	TC (mg/dl)	HDL-C (mg/dl)	Lipase Activity (U / L)	TG (mg/dl)	LDL-C (mg/dl)	Lip. A (mg/dl)
G1	After 4 weeks	72.63 ± 2.18^{d}	19.24 ± 1.27^{c}	68.11 ± 2.39^{b}	108.05 ± 5.53^{d}	31.77 ± 3.20^{c}	34.95 ± 2.54c
	After 8 weeks	76.32 ± 2.55^{d}	18.12 ± 1.12^{d}	55.65 ± 3.19^{b}	115.09 ± 4.43^{d}	35.18 ± 3.57^{b}	28.23 ± 2.65c
G2	After 4 weeks	67.91± 2.95^{d}	19.76 ± 1.19^{c}	58.82 ± 2.60^{c}	100.58 ± 5.45^{d}	26.05 ± 3.89^{d}	27.93 ± 2.33d
	After 8 weeks	61.88 ± 2.83^{e}	22.36 ± 1.08^{c}	47.91 ± 2.10^{c}	91.68 ± 5.08^{d}	21.19 ± 2.71^{c}	23.72 ± 1.72c
G3	After 4 weeks	56.09 ± 2.72^{e}	20.35 ± 1.32^{c}	44.91 ± 2.32^{d}	88.76 ± 3.94^{d}	17.98 ± 4.24^{d}	21.34 ± 1.46d
	After 8 weeks	51.40 ± 2.65^{e}	23.18 ± 1.41^{c}	36.68 ± 2.69^{d}	76.91 ± 3.91^{d}	12.84 ± 3.44^{d}	16.06 ± 1.55d
G4	After 4 weeks	188.51 ± 3.48^{a}	11.83 ± 1.54^{d}	116.90 ± 7.21^{a}	450.63 ± 15.64^{a}	86.55 ± 3.95^{a}	64.26 ± 4.87a
	After 8 weeks	235.71 ± 5.21^{a}	10.15 ± 1.40^{e}	136.92 ± 6.94^{a}	624.28 ± 21.44^{a}	100.71 ± 5.92^{a}	76.05 ± 6.41a
G5	After 4 weeks	145.45 ± 4.39^{b}	24.28 ± 2.27^{b}	72.88 ± 3.87^{b}	333.48 ± 9.81^{b}	54.48 ± 4.98^{b}	49.15 ± 3.75b
	After 8 weeks	126.70 ± 5.38^{b}	28.91 ± 2.87^{b}	58.80 ± 2.89^{b}	276.78 ± 12.15^{b}	42.44 ± 4.92^{b}	38.71 ± 3.58b
G6	After 4 weeks	121.23 ± 3.86^{c}	29.55 ± 2.49^{a}	58.36 ± 3.15^{c}	260.28 ± 9.45^{c}	39.64 ± 5.38^{c}	37.66 ± 2.67c
	After 8 weeks	102.22 ± 3.99^{c}	34.14 ± 2.36^{a}	46.87 ± 2.37^{c}	208.53 ± 9.06^{c}	26.37 ± 4.66^{c}	23.18 ± 2.48c

Data are expressed as (Mean ± S.E), S.E= standard error.

Mean values with different superscript letters in the same column are significantly different at : (P>0.05).

G1 = Control Group: received no drugs, provided only with a constant supply of standard pellet die for 8 weeks.

G2 = *Mimusops laurifolia* (Single dose) Group: provided with a constant supply of standard pellet die along with administration of *Mimusops laurifolia* (75.83 mg/kg b.wt.) for 8 weeks.

G3 = *Mimusops laurifolia* (double dose) Group: provided with a constant supply of standard pellet die along with administration of *Mimusops laurifolia* (151.66 mg/kg b.wt.) for 8 weeks.

G4 = High Fat Diet (HFD) Group: fed on high fat diet daily for 8 weeks; for induction of oxidative stress for 8 weeks.

G5 = HFD + *Mimusops laurifolia* (Single dose) Group: fed on high fat diet daily along with administration of *Mimusops laurifolia* (75.83 mg/kg b.wt.) for 8 weeks.

G6 = HFD + *Mimusops laurifolia* (double dose) Group: fed on high fat diet daily along with administration of *Mimusops laurifolia* (151.66 mg/kg b.wt.) for 8 weeks.

4.0 Discussion

Obesity and excess body weight (BW) are the most common nutritional disorders. It develops when energy intake consistently exceeds daily energy expenditure. **(Norris et al., 1993)**. Obesity and its complications represent one of the major emerging challenges for the developed world **(Fleming et al., 2013).** Hypertension,Cardiovascular disease and type 2 diabetes are common sequelae of obesity **(Calhoun et al., 2008).**

The obtained data showed that high fat diet feeding significantly increased serum total lipids TG and TC in HFD group compered to control normal group In all periods over the experiments.

These results were agreed with **(Bailhache et al., 2003)**, who mentioned that obese experimental beagles had higher total plasma triglyceride concentrations and lower VLDL and HDL triglyceride concentrations and lower HDL cholesterol concentrations compared with healthy beagles.

In another study performed by **(Isabelle et al., 2005)**, recorded that, obesity or high fat diet are associated with insulin resistance and that is associated with hyperlipidemia, a term used to describe an increase in plasma concentrations of cholesterol, triglycerides, or both which caused by defects in the metabolism of ≤ 1 of the lipoprotein classes. This was confirmed by results of **(Downs et al., 1997)**, in Labrador Retrievers which indicate that high-fat (20% to 25%) low-carbohydrate (26% to 33%) diets induce a significant increase in total plasma cholesterol concentration and in LDL cholesterol concentration, whereas a low-fat (13%) high-carbohydrate (44%) diet induces an increase in HDL triglyceride concentration.

(Balunas et al., 2005). stated that, plant natural products are a priceless source of medicinal compounds. Different classes of phytochemicals from these plants have been shown to modulate body weight. It has been demonstrated that polyphenols, modulate molecular pathways involved in energy metabolism **(Meydani et al., 2010)**. The anti-obesity properties of polyphenols may be due to their ability to interact with preadipocytes, adipose stem cells and immune cells of the adipose tissues **(Wang et al., 2014)** .

The obtained results revealed that, administration of *mimusops laurifolia* extract (at a dose of 80 and 160 mg/kg b.wt.) to HFD-stressed rat groups lead to significant decrease in serium TC, TG concentrations when compared to group fed with HFD only. These results were nearly similar to that recorded by **(Ghaisas et al., 2008)**, who found that administration of ethanolic extract of *Mimusops elengi* L. (ME) at a dose of 100, 300, 600 mg/ kg, b. w. to Triton WR-1339 induced hyperlipidemic rats showed significant reduction in levels of TG and TC after 7 and 24 hours of induction, moreover, HDL level was significantly elevated in groups of ME 300, ME 600 respectively after 7 and 24 h. Similarly , **(Hina et al., 2012)**, investigated the adminstration of methanolic extracts of flower and leaves (MFE) and (MLE) of *Mimusops elengi* Linn (sapotaceae) at a dose of 100 mg/kg b. w. to normoglycaemic and alloxan-induced diabetic rats showed marked decrease ($P < 0.01$) in TG levels after 7 days compared to the diabetic control group. and attribute the decrease in cholesterol and triglyceride by MLE might be directly or indirectly related with the decreased of blood glucose levels in alloxan induced diabetic rats which may be due increased sensitivity of

insulin receptors or increase in the protective/ inhibitory effect against insulinase enzyme **(Mostofa et al., 2007)**.

(Guimaraes et al., 2002) recorded that the plant constituents like steroids, flavonoids, saponins are reported to possess lipid lowering activity and reduce the absorption of cholesterol and thus increase feacal excretion of cholesterol. **(Fukusrma and Mastuda, 1997)** mentioned that, Saponins act as antihyperlipidemic by binding with cholesterol in intestinal lumen, so that cholesterol is less readily absorbed and besides increasing lipoprotein lipase activity which helps in removal of VLDL and chylomicrons from circulation.

Our results revealed that high fat diet feeding significantly increase LDL-c whereas, significantly decrease serum HDL-c in HFD group compared with all other groups along the total period of the experiment. **(Magkos et al., 2008)** found that obesity, even in the absence of clinically significant imbalances in glucose and lipid homeostasis, was associated with a 50–100% increase in the concentrations of the pro-atherogenic lipoproteins VLDL, IDL and LDL, as well as a small, and biologically probably insignificant, increase (by B10%) in HDL particle concentration.

Moreover, previous research has shown that hypercholesterolemia, low high-density lipoprotein cholesterol (HDL-c) levels and elevated low-density lipoprotein cholesterol (LDL-c) levels are prerequisites for atherogenesis **(Alberti et al., 2006)**. and people with elevated LDL-c levels are at higher risk for CVD **(Soeki et al., 1999)**.

(Balunas et al., 2005) hypothesized that, prolonged exposure to elevated FFA leads to increased HDL-c synthesis and concomitantly, an increase in LDL-c, which ultimately get released into the arterial system and deposited to trigger atherogenesis .
Similarly, **(Luo et al., 2014)** found that elevated LDL-c and ApoB levels were associated with increases in Body mass index (BMI) and increased measured Visceral fat area (VFA).

On the other hand **(Brown et al., 2000)** suggested that, the prevalence of low HDL-c among overweight and obese individuals is variable. Where obese people with a BMI> 30, the prevalence of low HDL-c (<45 in women and <35 mg/dl in men) is 40.6% In women and 31.1% In men cc

in this respect, **(Mooradian et al., 2007)** stated that, Low plasma HDL-C level in obesity can occur in the presence or absence of hypertriglyceridemia. It is estimated that 50% of obese people without hypertriglyceridemia have reduced HDL-c . One of the principal properties of HDL is that it has scavenging toxic by-products of LDL oxidation such as lysophosphatidylcholine, Anti-thrombotic and fibrinolytic activity through promotion of protein C, and inhibition of LDL retention **(Hachem et al., 2006).**

the results revealed that administration of *mimusops laurifolia* extract (at a dose of 80 and 160 mg/kg b.wt.) to HFD-stressed rat groups lead to significantly decrease LDL-c whereas, significantly increase serum HDL-c in compared with HFD group along the total period of the experiment.

These results are in a harmony with that of the experement performed by **(Ghaisas et al., 2008)**, who observed that hyperlipidimic groups induced by 100 mg/kg Triton WR-1339 and treated by methanolic extracts of the leaves of *M. elengi* at 300 and 600 mg/kg body weight, p.o.showed significantly elevated HDL level after 7 and 24 h of induction.

Furthuremore, **(Devi and Sharma, 2004)** revealed that, flavonoids augment the activity of lecithin acyl transferase (LCAT) which regulates blood lipids and play a role in the incorporation of cholesterol into HDL (this may increase the level of HDL). Several studies have showed that increase in HDL is associated with decrease in cardiovascular diseases.
(Rajiv et al. 2011) detect and quantify quercetin from *Mimusops elengi* L. leaves using high performance thin Layer chromatography and obtain 19.191 mg/g quercetin in powdered leaf sample. **(Ziaee et al., 2009)** reported that, oral administration of quercetin to rats fed a high cholesterol diet result in a decrease in serum levels of LDL- and VLDL-cholesterol, together with the induced decrease of HMG-CoA activity and the increase of plasma LPL and LCAT .

Data represented revealed that high fat diet feeding significantly increase serum Lipase Activity and serum Lip.A concentration in HFD group compered to control normal group In all periods over the experiments. **(Klop et al., 2013)** showed that, hepatic lipase activity is increased in patients who are obese with increased visceral adiposity, which will facilitate the removal of triglyceride from LDL and HDL resulting in formation of small dense lipoprotein particles which are more toxic and atherogenic**.**

On the other hand, **(Bays et al., 2013)** showed that, the triglyceride on LDL and HDL is hydrolyzed by hepatic lipase and lipoprotein lipase leading to the production of small dense LDL and small HDL particles

(María et al., 2015) reported that feeding rabbits for 50 days with diets containing 5.9% diet rich in cholesterol and lard increased lipase activity in the pancreas significantly supporting the view that adaptation of this enzyme depends on both the amount of fat and the length of the feeding period which may be due to increase Simulation of mRNA transcription and increase synthetic rate of enzyme protein. A positive correlation was observed between Lp(a) and LDL cholesterol (LDL-c), Lp(a) and total cholesterol (TC) and Lp(a) and apolipoprotein B (Apo B), which suggests an association between Lp(a) levels and lipid profile **(Sáez de Lafuente et al., 2006)**. According to **(Meabe et al., 2006)**, the fact that high Lp(a) levels are associated with high LDL-c levels proposes that the LDL metabolism may be involved in the Lp (a) synthesis.

Lp(a) has LDL-like properties and it has been hypothesized that elevated Lp(a) could increase the risk for atherosclerosis. In support of this idea, studies performed by **(Onat et al., 2013)** have found that individuals with high Lp(a) levels are more Likely to develop CVD .

Our results revealed that administration of *mimusops laurifolia* extract (at a dose of 80 and 160 mg/kg b.wt.) to HFD-stressed rat groups lead to significant decrease in lipase activity and serum (Lip.A) concentration in compared with HFD group along the total period of the experiment. Our results were in accordance with the study of **(Prashith et al., 2014)** who investigate the inhibitory effect of methanolic leaves extract of *Chrysophyllum roxburghii*, a plant species in the family *Sapotaceae* belonging to the genus*: mimusops*, and Orlisat (reference standard drug) against lipase extracted from the pancreas of chicken and found

that the leaf extract inhibit the activity of chicken pancreatic lipase in a dose dependent manner. Higher inhibition of enzyme (>50%) was observed at extract concentration 50mg/ml of a variety of samples.

The observed bioactivities of leaf extract could be ascribed to the presence of secondary metabolites namely of tannins, alkaloids and terpenoids.

(Mariangela et al., 2016) established that, pancreatic lipase is the most important lipase and is associated with the hydrolysis of 50%–70% of total dietary fats. Lipase inhibition is one of the most important strategies advanced by pharmaceutical industries to decrease fat absorption after its ingestion. According to the world health organization (WHO), medicinal plants are important tools for healthcare Nowadays, since synthetic anti-obesity drugs are characterized by important side effects, we are currently assisting to increase the scientific interest towards natural products.

(Karu et al., 2007) assayed the effects of the saponin fraction extracted from the roots of one of herbal plants, panax ginseng CA Meyer, on obese male Balb/c mice induced by a high-fat diet. Ginseng saponins were able to reduce the adipose tissue weights and inhibit pancreatic lipase activity in a dose dependent manner compared to the high fat diet control group.

5.0 Conclusion and recommendation

In the present study, it can be concluded that *Mimusops laurifolia* butanolic Leaves extract has significant hypolipidimic effects against hperlipidemia induced by high fat diet in rats, owing to its ability to reduce levels of total cholesterol, triglyceride, LDL-C, (Lip. A) and lipase activity but increasing HDL levels. These effects may be attributed to active constituents present in *Mimusops laurifolia* as triterpenes and saponins. Further studies are needed to elucidate possible biochemical mechanism.

References

Amir., F., Wong, K., C., Eldeen, I., M., Asmawi, M., Z., Osman, H.2012. Volatile constituents and bioactivities of *Mimusops elengi* flowers. Latin American Journal of Pharmacy,;31 (2): 331-335.

Alberti, K., G., Zimmet, P., Shaw, J.2006. Metabolic syndrome–a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabetic medicine: a journal of the British Diabetic Association 23: 469–480.

Azevedo, A., Santos, A., C., Ribeiro, L. and Azevedo, I.2009. The metabolic syndrome in Oxidative Stress, Inflammation and Angiogenesis in the Metabolic Syndrome. R. Soares and C. Costa, Eds., pp. 1–19, Springer Science, Nerw York, NY, USA.

Balunas, M., J., Kinghorn, A.,D.2005. Drug discovery from medicinal plants. Life Sci. 78, 431–441.

Bailhache, E., Nguyen, P., Krempf, M., et al. 2003. Lipoproteins abnor- malities in obese insulin-resistant dogs. Metabolism;52:559-564.

Burstein M, Scholnick HR, Morfin R.1970. Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. J Lipid Res. 1970 Nov;11(6):583-95.

Brown., C., D., Higgins, M., Donato, K., A et al. 2000. Body mass index and the prevalence of hypertension and dyslipidemia. Obes Res;8:605-619.

Bays, H.E., et al. 2013. Obesity, adiposity, and dyslipidemia: a consensus statement from the National Lipid Association. J Clin Lipidol; 7(4): p. 304-83.

Calhoun, D.,A., Jones, D., Textor S., Goff, D.,C., Murphy, T.,P., Toto, R.,D., White, A., Cushman, W.,C., White, W., Sica, D., Ferdinand, K., Giles, T.,D., Falkner, B., Carey, R.,M. . 2008. American Heart Association Professional Education Committee. Resistant hypertension: diagnosis, evaluation, and treatment: a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research.Circulation. 117:510–526.

Downs, L., G., Crispin, S., M., Le Grande-Defretin, V, et al. 1997. The effect of dietary changes on plasma lipids and lipoproteins of six Labrador retrievers. Res Vet Sci 1997;63:175-181.

Epstin, F., M.1992. New England J.Medi., 122-123**.**

Enas, A., E., Chacko, V., Senthilkumar, A., Puthumana, N., Mohan, V. 2006. Elevated lipoprotein(a) – a genetic risk factor for premature vascular disease in people with and without standard risk factors: a review. Dis Mon; 52:5-50.

Fleming, Ng, Robinson, M., T., M., et al. 2013. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study.Lancet. 2014; 384:766–781.

Friedewald, W., T., Levy, R., I., Fredrickson, D., S.1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge . Clin Chem; 18: 499-502.

Fukusrma, M., Mastuda. 1997. Lipids.32: 1069-1071.

Ghaisas, M.M, Kadam, A., H., Kshirsagar, B., D., Dhote, V & V., Deshpande, A., D. 2008. Evaluation of Antihyperlipidemic activity of *Mimusops elengi* L. in Triton WR- 1339 hyperlipidaemia in rats. Journal of Natural Remedies, Vol. 8/2 () 132- 137 .

Guimaraes, P.,R., Galavao, A., M., Batista, C., M. 2002. Braz. J. Med. Bio. Res., 33:1022-1027.

Gami., B., Pathak, S., Parabia, M. 2012. Ethnobotanical, phytochemical and pharmacological review of *Mimusops elengi* Linn. Asian Pacific journal of tropical biomedicine; 2(9): 743-748.

Grundy, S., M.2002. Obesity, metabolic syndrome and coronary atherosclerosis. Circulation;105:2696–2698.

Hina, Zahid, Ghazala, Hafeez, Rizwani, Huma, Shareef, Shaukat, Mahmud and Tahir Ali.2012. Hypoglycemic and Hypolipidemic Effects of *Mimusops elengi* Linn Extracts on Normoglycaemic and Alloxan-Induced Diabetic Rats. International Journal of Pharmaceutical & Biological Archives 3(1):56-62 4 J.

Hachem, S., Mooradian, A., D., Familial.2006. dyslipidemias: an overview of pathophysiology and management. Drugs 66:1949-1969.

Isabelle., C., Jeusette, D., V., M., Estelle, T., Lhoest, D., V., M., Louis, P., Istasse, , D., V., M., PhD, Marianne, O., Diez, D., V., M., PhD. 2005. Influence of obesity on plasma lipid and label protein concentrations in dogs. Animal Nutrition Unit, Veterinary Faculty, B43, University of Liege, B-4000 Liege, Belgium. (AJVR), Vol 66, No. 1.

Karu, N., Reifen, R., Kerem, Z. 2007. Weight gain reduction in mice fed Panax ginseng saponin, a pancreatic lipase inhibitor. J. Agric. Food Chem., 55, 2824–2828.

Kastelein, JJ, van der Steeg, W., A., Holme, I., Gaffney, M., Cater, N.,B. et al.2008. Lipids, apolipoproteins, and their ratios in relation to cardiovascular events with statin treatment. Circulation 117: 3002–3009.

Kew. 2013."Chrysophyllum roxburghii". Royal Botanic Gardens.

Klop, B., J., W., Elte and Cabezas, M., C. 2013. Dyslipidemia in obesity: mechanisms and potential targets.Nutrients, 5(4): p. 1218-40.

Khan, M., d., Yaqub, Poonam, Gupta, Bipin, Bihari, Aparna, Misra, Ashish, Pathak, Vikas, Kumar, Verma. 2012. A Review on Obesity and its Management. International Journal of Scientific & Engineering Research, Vol. 3: 11, - 2ISSN 2229-5518.

Kirtikar, K., R., Basu, B., D. 2004. Indian Medicinal Plants. International Book Distributors, Deharadun: 2067-2070.

Laclaustra, M., Corella, D., and Ordovas, J., M. 2007. "Metabolic syndrome pathophysiology: the role of adipose tissue," Nutrition, Metabolism and Cardiovascular Diseases. vol. 17, no. 2, pp. 125–139.

Lee, E., T., Wang, W., Alaupovic, P., Blackett, P., Blevins, K., S. 2005. Correlation between lipoprotein(a) and other risk factors for cardiovascular disease and diabetes in cherokee indians: the Cherokee Diabetes study. Ann Epidemiol;15:390-7.

Liu., T., Li, Z., Wang, T., Zhu, X.2016. Effects of Alfalfa Saponins on Cholesterol Metabolism in Broilers. J Nutr Food Sci 6:546. doi:10.4172/2155-9600.1000546.

Luo, Yuqi, Xiaojing, M., a., Yun, Shen, Yaping, Hao, Yaqin, Hu, Yunfeng, Xiao, Yuqian, Bao, Weiping, Jia.2014. Positive Relationship between Serum Low-Density Lipoprotein Cholesterol Levels and Visceral Fat in a Chinese Nondiabetic Population. PLOS ONE 9(11): e112715.

Magkos., F., Mohammed, B.,S and Mittendorfer, B. 2008. Effect of obesity on the plasma lipoprotein subclass profile in normoglycemic and normolipidemic men and women. International Journal of Obesity 32; 1655–1664

María Alba, Martinez, BURGOS, Maria Dolores, Yago TORREGROSA, Maria Dolores, Mesa GARCIA, María Belén, López MILLAN, Jesús Alcalá Bejarano, CARRILLO, Ana Rivas, VELASCO, Angel Gil HERNÁNDEZ, ALMENDROS. 2015. Effects of a Western-style diet high in cholesterol and on the rabbit exocrine pancreas. Turkish Journal of Biology Vol; 39: 765-774 .

Mariangela, Marrelli, Filomena, Conforti, Fabrizio, Araniti and Giancarlo, A., Statti. 2016. Effects of Saponins on Lipid Metabolism: A Review of Potential Health Benefits in the Treatment of Obesity. Molecules, 21,1404;

Maxwell, C., J., Obisesan, T., O., Aliyu, M., H., Adediran, A., S., Bond, V., Rotimi, C., N. 2004. Correlates of serum lipoprotein (A) in children and adolescents in the United States. National Health Nutrition and Examination Survey (NHANES III). Lipids Health Dis; 3:1-10.

Meabe, Y., S., Bernar, M., L., Chivite, J., P., Gofinondo, I., N., Rius, M., V., López, A., M et al. 2006. Correlación de los perfiles lipoproteicos y variables antropométricas con concentraciones séricas de lipoproteína(a) en la infancia. An Pediatr (Barc);64:235-8.

Meydani, M., Hasan, S.,T. 2010. Dietary polyphenols and obesity. Nutrients, 2, 737–751.

Monteiro, R., Azevedo, I. 2010. Chronic inflammation in obesity and the metabolic syndrome. Mediators. Inflamm., 289645.

Molla, M.; Gemeda, N.; and Abay, S.M. 2017. Investigating Potential Modes of Actions of *Mimusops kummel* Fruit Extract and Solvent Fractions for Their Antidiarrheal Activities in Mice. Evidence-Based Complementary and Alternative Medicine Volume 2017, Article ID 4103410, 11 pages.

Mooradian., A., D., Albert, S., G., Hass, M., J. 2007.Low serum HDL cholesterol in obese subjects with normal serum triglycerides: the role of insulin resistance and inflammatory cytokines. Diabetes Obes Metab;9:441-443.

Moss DW, Henderson AR. Digestive enzymes of pancreatic origin.In: Burtis CA, Ashwood ER, editors. Tietz Textbook of Clinical C.

Mostofa, M., Choudhury, M.,E., Hossain, M.,A., Islam, M.,Z., Sumon, M.,H. 2007. Antidiabetic effects of Catharanthus roseus, Azadirachta indica, Allium sativum and Glimepride in experimentally diabetic induced rat. Bang J. Veterinary Med vol:5(1&2): 99-102.

Mota, A., P., Carvalho, M., G., Lima, L., M., Santos, M.,E., Sousa, M.,O. 2008. Lipoprotein (a) in patients with peripheral arterial obstructive disease and/or type 2 diabetes mellitus. J Bras Patol Med Lab;44:89-95.

Norris, M. P., Beaver, B. V. 1993. Application of behavior therapy techniques to the treatment of obesity in companion animals. J Am Vet Med Assoc;202:728–730.

Onat, A., Can, G., Ornek, E., Sansuy, V., Aydin, M., et al. 2013. Abduminal obesity with hypertriglyceridaemia, lipoprotein(a) and apolipoprotein A-I determine marked cardiometabolic risk. European journal of clinical investigation 43 1129-1139.

Prashith, Kekuda, T., R., aghavendra., H., L., Mallikarjun, N., Swathi., D., Suchitha, Y., Anil., Kumar., HS3 and Vinayaka, K., S. 2014. Elemental Analysis and Biological Activities of Chrysophyllum roxburghii G. Don (Sapotaceae) Leaves.Sci. Technol. Arts Res. J., Jan-March, 3(1): 14-20.

Rajiv Gupta, Sakshi, Sehgal, Vineet, Gupta, Shubhini, A., Saraf. 2011. Quantitative Estimation of Quercetin in *Mimusops elengi* L. (Bakul) Leaves by HPTLC. Der Pharmacia Lettre: 3 (5)12-19.

Rout, P., K., Sahoo, D., Misra, L., N. 2010. Comparison of extraction methods of *Mimusops elengi* L. flowers. Industrial crops and Products 32(3); 678-680.

Rastogi, R., P., Mehrotra, B., N. 1999. Compendium of Ind. Medi. Plants. Central Drug Research Institute, Luknow and National Institute of Science Communication, New Delhi: 479- 480.

Sáez de Lafuente, J., P., Sáez Y., Vacas M., Lafita, M., Narváez I., Santos, M., et al. 2006. Lipoproteína(a), variables antropométricas, parámetros lipídicos y trombogénicos en la infancia. Clin Invest Arterioscl;18:82-8.

Searcy.R.L., (1969). Diagnostic Biochem.McGraw-Hill,New York,NY.

Shah, P.J., M.S. Gandhi, M.,B., Shah, SS, Goswami and D., Santani. 2003. Study of *Mimusops elengi* bark in experimental gastric ulcers. J. Ethnopharmacol. 89: 305-311.

Soeki, T., Tamura, Y., Shinohara, H., Tanaka, H., Bando, K., et al.1999. Fibrinolytic factors, serum lipid and C-reactive protein predicting cardiac events in Japanese patients with coronary atherosclerotic lesions. Japanese circulation journal 63: 976–980.

Steel, R., Torrie, J. and Dickey, D.1997. Principles and procedures of Statistics: A Biometrical Approach, 3rd ed., McGraw-Hill, New York, NY.

Stein, E., A.1987. Lipids, Lipoproteins and apolipoproteins. Fundementals of clinic chem.3rd Ed: 448-4481. Philadelphia: WB Saunders.

Sundari, U., T., Rekha, S., Parvathi, A. 2012. Phytochemical analysis of some therapeutic medicinal flowers. International Journal of Pharmacy; 2(3): 583-585.

Wang, S., Moustaid-Moussa, N., Chen, L., Mo., H., Shastri, A., Su., R., Bapat, P., Kwun, I., Shen, C.-L. 2014. Novel insights of dietary polyphenols and obesity. J. Nutr. Biochem. 2014, 25, 1–18.

Xue, Xin, Zhonghua, Guan, Bing, Za, Zhi. 2007.Chinese guidelines on prevention and treatment of dyslipidemia in adults. Joint committee for developing Chinese guidelines on prevention and tretment of dyslipidemia in alduts 35: 390–419.

YH, Yu, 1990. Feed toxicology report of toxicology. Beijing: Agricultural Publishing House pp: 16-45.

Yu, CH, Xie, G., He, RR, Zhai, Y., J., Li, Y., F., et al.2011. Effect of a purified saponin mixture from alfalfa on plasma lipid metabolism in hyperlipidemic mice. J Health Sci 57: 401-405.

Ziaee, A., Zamansoltani, F., Nassiri-Asl, M., Abbasi, E. 2009. Effects of rutin on lipid profile hypercholesterolaemic rats. Basic Clin. Pharmacol. Toxicol. 104; 253-258.