IJPSR (2018), Volume 9, Issue 9 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 08 January, 2018; received in revised form, 04 March, 2018; accepted, 11 March, 2018; published 01 September, 2018

DYSLIPIDEMIC AND PROTECTIVE EFFECTS OF ASPIRIN AND CLOPIDOGREL IN OBESE RATS

Doa'a Anwar Ibrahim

Department of Pharmacology Unit, Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, University of Science and Technology, Sana'a, Yemen.

Keywords:

Aspirin, Clopidogrel, Dyslipidemic and Protective effects, Obese rats

Correspondence to Author:
Doa'a Anwar Ibrahim

Associate Professor,
Department of Pharmacology Unit, Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, University of Science and Technology, Sana'a, Yemen.

E-mail: dr_d_anwar@hotmail.com

ABSTRACT: Introduction: Antiplatelets play a crucial role in improving many metabolic disorders and complications, including dyslipidemia, atherosclerosis, diabetes mellitus and cardiovascular diseases. The most common and effective antiplatelets used widely are aspirin and clopidogrel. The aim of this study is to evaluate the dyslipidemic and protective effects of aspirin and clopidogrel in obese rats. **Materials and methods:** 24 rats were divided into two groups, control (n = 6) (was taken normal chow) and the other group (n = 18) were allowed to eat beef tallow (90 g) and saturated fat (10 g) for 6 weeks to induce obesity. The second group was further classified to three subgroups, subgroup I (n = 6) was kept as obese group (n = 6) (positive control), subgroup II (n = 6) obese rats were treated with aspirin and subgroup III (n = 6) obese rats were treated with clopidogrel for 7 days. At the end of experiment blood samples were taken and lipid profile, FBS measured as well as body weight and the relative weights of liver were calculated. Histopathological samples were taken from different organs including liver, kidneys and heart. **Results:** Outcomes of this study showed that both tested drugs had dyslipidemic and protective effects as they significantly reduced cholesterol, TG, FBS as well as body and liver weight. They also ameliorated obesity-induced abnormalities in histopathological tissues with slight differences between the tested groups. **Conclusion:** It suggested from the findings of this study that both aspirin and clopidogrel might have dyslipidemic and protective effects in obese rats supported by histopathological findings.

INTRODUCTION: Cardiovascular diseases are among the highest causes of the morbidity and mortality in developed and developing countries [1]. Obesity is the major risk factor of cardiovascular diseases, diabetes mellitus, hypertension and dyslipidemia [2]. Dyslipidemia namely lipoprotein is the root cause of atherosclerosis.

QUICK RESPONSE CODE

DOI:
10.13040/IJPSR.0975-8232.9(9).3647-55

Article can be accessed online on:
www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.9(9).3647-55

The beginning process is started when the lipoprotein migrated from the endothelial cells to the arterial wall, where they are modified by oxidation [3]. However, the endothelial cell layer has anticoagulant phenotype and the blood cells, platelets and clotting factors that are travelling there without adhesion. When an injury or physical trauma of blood vessels is occurring hemostasis cascade is begun. Platelets are the central in normal hemostasis and thromboembolic diseases, that monitoring the integrity of endothelium [4]. In addition, different substances regulate the function of platelets. These are prostacyclin, prostaglandin E2, ADP, thromboxane A2, cAMP.

Aspirin and clopidogrel are the most common antiplatelets through inhibition of some of these substances mainly thromboxane A2 and ADP. These are decrease the formation or the action of chemical signals that promote platelet aggregation [5]. Aspirin inhibits the thromboxane A2 synthesis from arachidonic acid in platelets by irreversible acetylation of a serine, thus will prevent binding of arachidonic acid to the active site resulted in inhibition of COX-1. It is currently used in the prophylactic treatment of transient cerebral ischemia, to reduce the incidence of recurrent myocardial infarction, and to decrease mortality in pre- and post-myocardial infarct patients [6]. Other salicylates and nonsteroidal anti-inflammatory drugs also inhibit cyclooxygenase but have a shorter duration of inhibitory action because they cannot acetylate cyclooxygenase; that is, their action is reversible [7].

On the other hand, clopidogrel reduced platelet aggregation through the inhibition ADP pathway of platelets. Unlike aspirin, clopidogrel inhibits irreversibly ADP receptors on platelets and, thereby, inhibits the activation of the GP IIb/IIIa receptors required for platelets to bind to fibrinogen and to each other [8]. Clopidogrel is approved for prevention of atherosclerotic events following recent myocardial infarction, stroke, and established peripheral arterial disease. Additionally, it is also used for preventing ischemic heart disease and as prophylaxis of thrombotic events in acute coronary syndrome (unstable angina) [9].

MATERIALS AND METHODS:

Drugs: Aspirin and clopidogrel were purchased from Bayer and Bristol-Myers Squibb respectively. They are commonly used as effective antiplatelet agents. Each of them was dissolved in 2 ml normal saline.

Animals: Wister albino rats (*Rattus norvegicus* Albinus) with weight (180 ± 20 g) were brought from Biology Department- Sana'a University. They were left to acclimatize in 12 h dark/light cycle with room temperature 25 ± 2 °C for one week with free access of water and normal rats chow.

Induction of Obesity: Twenty-four male rats were divided into two groups randomly, control (n = 6) (was taken normal chow) and the other group (n = 18) were allowed to eat beef tallow (90 g) and saturated fat (10 g) that contained (wheat flour base with addition of egg yolk, dried milk, sugar, salt and palm oil) for 6 weeks to induce obesity. The average consumption of diet 100 g / rat per day.

Study Design: After 6 weeks, the second group (obese) n = 18 was classified into three subgroups. Subgroup I (n = 6) was kept as an obese group (n = 6) (positive control) taken only 2 ml of normal saline, subgroup II (n = 6) obese rats were treated with aspirin (25 mg/kg) and subgroup III (n = 6) obese rats were treated with clopidogrel (25mg/kg) for 7 days [10]. All tested drugs were given through oral gavage.

The University Ethics Committee approved all the experiment's steps before commencing the experiment (MECA no. 2017/07). At the end of the experiment, blood samples were taken from retro-bulbar area to measure lipid profile (cholesterol, TG) [11, 12] and FBS [13]. Body weights of control, obese and treated groups before and after treatment were taken and the relative weights of liver were calculated. Histopathological samples from different groups were taken from different organs including liver, kidneys and heart to assess the harmful effects of obesity on these important organs and to assess the beneficial and protective effects of the tested drugs.

Histopathological Study: In the last day of this study, animals were undergone with light anesthesia with halothane and sacrificed. The organs (heart, liver and kidneys) were removed and washed carefully and kept in 10% formalin fixative. Then prepared in wax blocks for cutting to thin sections by using a microtome to get 5 µ thickness of that sections. Then they stained with Eosin and haematoxylin and examined to detect any histopathological changes. The aim of this study is to evaluate the dyslipidemic and protective effects of the two effective anti-platelets agents: aspirin and clopidogrel on obese rats.

Statistical Analysis: All data were expressed as Mean ± SEM by using the Statistical Analysis (SPSS) Software Package version 21. One-way variance (ANOVA) was used and the comparison between groups done by the Tukey Post Hoc - test. The values were considered significant if $P < 0.5$.

RESULTS: The outcome of this study indicated that there is a significant increase in mean body weight after 6 weeks intake high fat diet in the obese group compared with the control group. Additionally, there is no significant change between treated groups either by aspirin or by clopidogrel compared with the obese group after 7 days of continuous treatment as shown in **Table 1**.

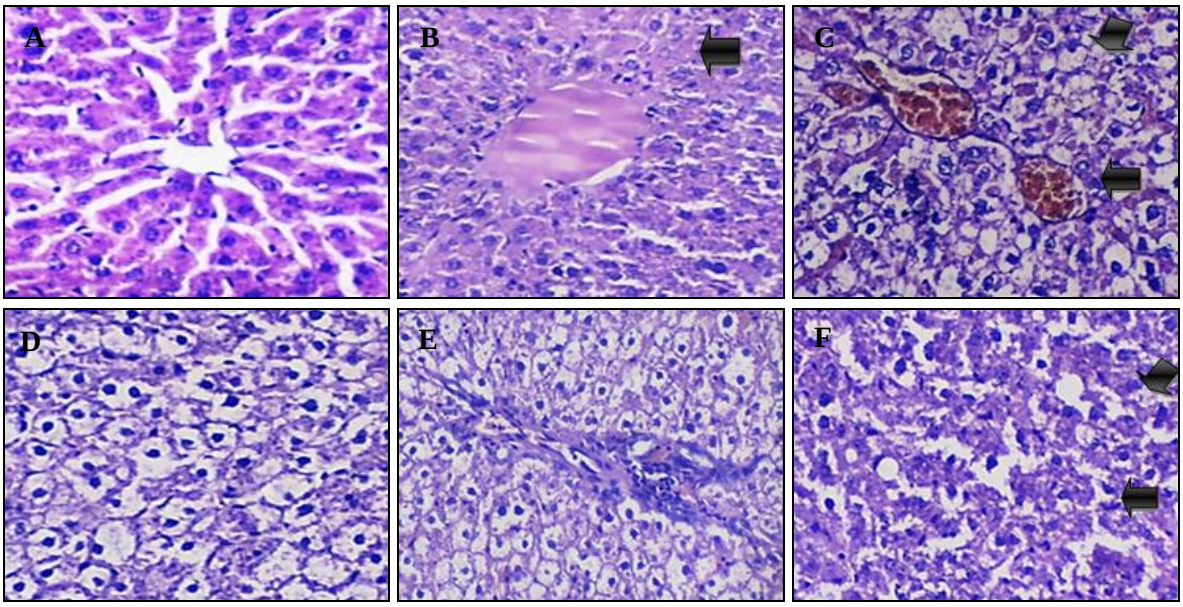

FIG. 1: PHOTOMICROGRAPH OF THE RAT LIVER SECTIONS (OBESE) SHOWED (A): NORMAL HEPATOCYTES ARCHITECTURE WITH NORMAL CENTRAL VEIN AND NORMAL HEPATOCYETS. (B): AMYLOID (C): CONGESTED CENTRAL VEIN AND HYDROPIC CHANGES. (D): SEVER HYDROPIC CHANGES. (E): INFLAMMATORY CELLS INFILTRATION WITH HYDROPIC CHANGES. (F): FATTY CHANGES

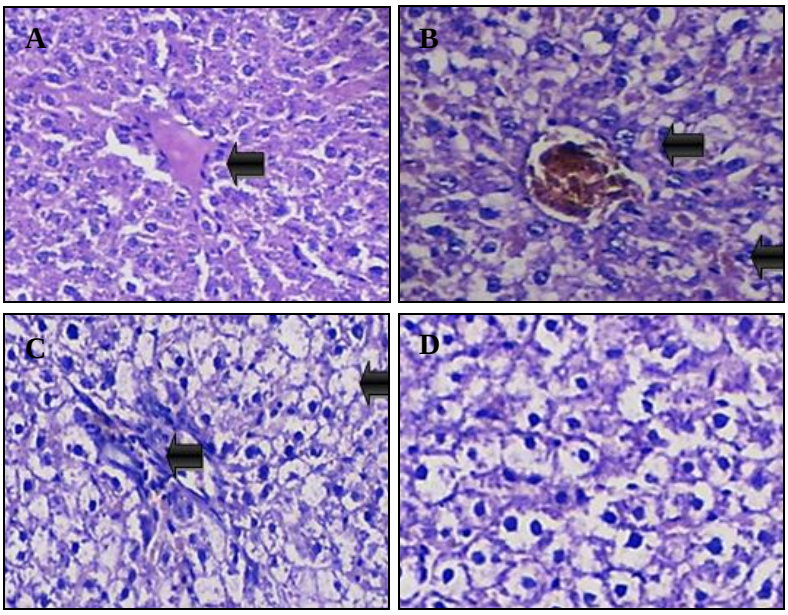

FIG. 2: PHOTOMICROGRAPH OF THE RAT LIVER SECTIONS (TREATMENT WITH ASPIRIN) SHOWED (A): SLIGHT RECOVERY FROM AMYLOID. (B): SLIGHT RECOVERY FROM CONGESTION AND HYDROPIC CHANGES (C): SLIGHT RECOVERY FROM INFILTRATION AND HYDROPIC CHANGES. (D): SLIGHT RECOVERY FROM RECOVERY FROM

According to lipid profile and fasting blood sugar results, obese group showed significant increase $P < 0.05$ compared with the control group. Contradictory, treated groups with aspirin and clopidogrel produced significant $P < 0.05$ reduction in the previous parameters compared with the obese group with slight improvement in the clopidogrel compared with aspirin as shown in **Table 2.**

TABLE 1: EFFECT ASPIRIN AND CLOPIDOGREL ON (MEAN ± SEM) BODY WEIGHT AND RELATIVE WEIGHT OF LIVER IN MALE RATS (N = 6)

Parameters	Mean ± SEM			
	Control	Obese animal	Aspirin	Clopidogrel
B. wt. (g) before	192.3 ± 6.12	279.8 ± 14.3*	271.8 ± 5.30	263.3 ± 12.7
B. wt. (g) after	203.3 ± 4.60	286.2 ± 15.3*	264.5 ± 9.17	268.8 ± 15.8
Weight of liver (g)	7.267 ± 0.667	13.95 ± 0.154*	11.0 ± 0.98**	10.53 ± 1.29**
Relative wt. of liver	3.6	4.9*	4.1**	4.0**

*Significant as compared with control at (P< 0.05), ** significant as compared with obese group at (P< 0.05)

With regard to the histopathological studies of both treated groups. It was found that clopidogrel showed more beneficial effects on different body tissues that taken from rat liver, kidneys as well as heart compared with obese and aspirin treated groups as shown in **Fig. 1, 2, 3, 4, 5, 6, 7, 8** and **9**.

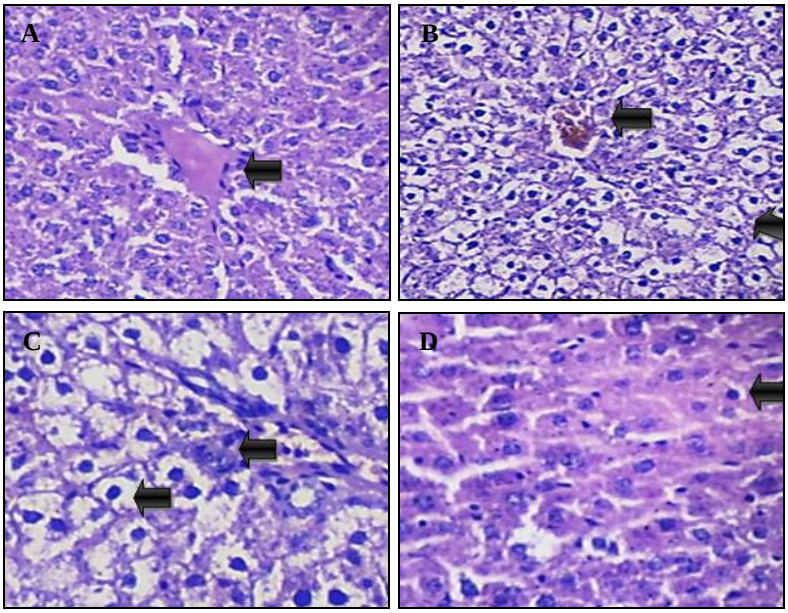

FIG. 3: PHOTOMICROGRAPH OF THE RAT LIVER SECTIONS (TREATMENT WITH CLOPIDOGREL) SHOWED (A): MILD RECOVERY FROM AMYLOID. (B): MILD RECOVERY FROM CONGESTION AND HYDROPIC CHANGES (C): MILD RECOVERY FROM INFILTRATION AND HYDROPIC CHANGES. (D): MILD RECOVERY FROM FATTY CHANGES

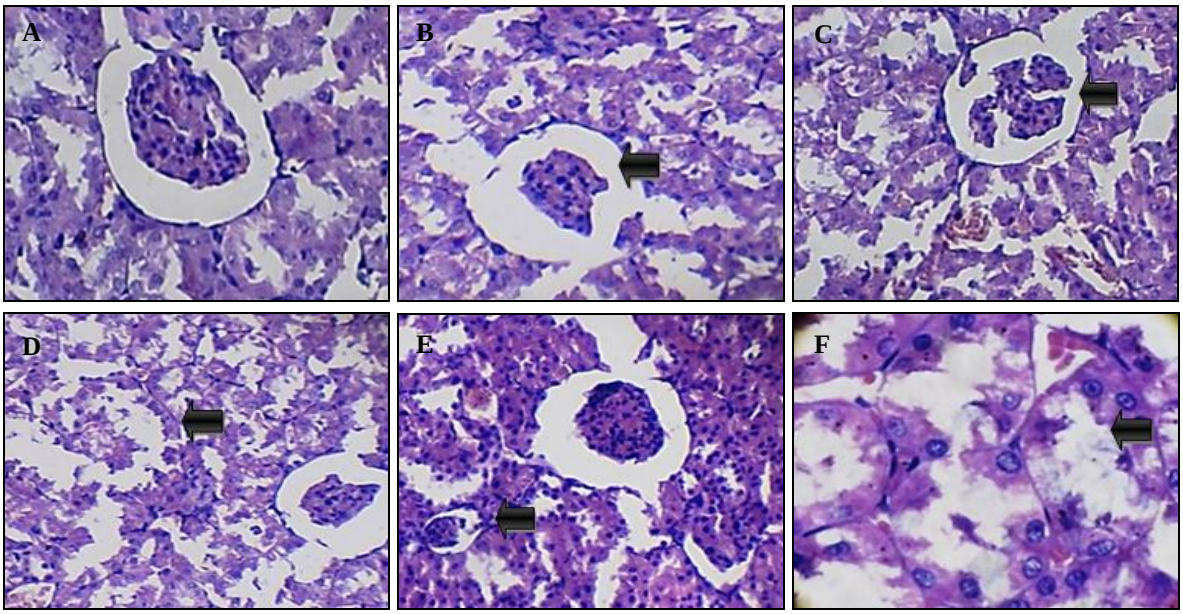

FIG. 4: PHOTOMICROGRAPH OF THE RAT KIDNEY SECTIONS (OBESE RATS) SHOWED (A): NORMAL GLOMERULUS WITH NORMAL TUBULES. (B): SHRINKED GLOMERULUS (C): DEGENERATED GLOMERULUS. (D): DEGENERATED RENAL TUBULES. (E): ATROPHOID GLOMERULUS. (F): NECROTIC RENAL TUBULES

TABLE 2: EFFECT ASPIRIN AND CLOPIDOGREL ON (MEAN ± SEM) LIPID PROFILE AND FBS IN MALE RATS (N = 6)

Parameters	Mean ± SEM		
	Cholesterol (mg/dl)	TG (mg/dl)	FBS (mg/dl)
Control	97.25 ± 2.43	68.5 ± 4.57	94.5 ± 2.75
Obese animal	155.0 ± 18.41*	422.25 ± 46.9*	260.5 ± 44.2*
Aspirin	123.5 ± 4.17**	239.2 ± 2.17**	150.2 ± 27.1**
Clopidogrel	118.0 ± 6.16**	226.3 ± 47.8**	142.5 ± 47.8**

*Significant as compared with control group at (P< 0.05), ** significant as compared with obese group at (P< 0.05)

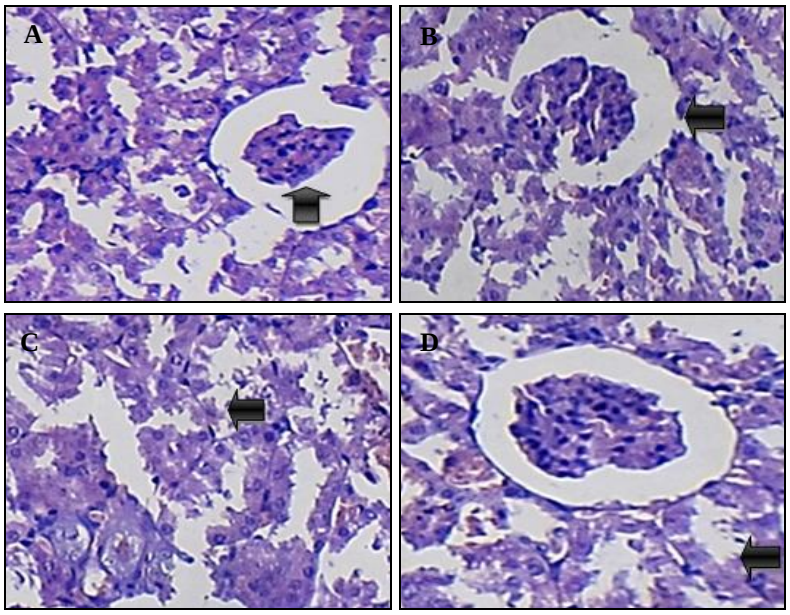

FIG. 5: PHOTOMICROGRAPH OF THE RAT KIDNEY SECTIONS (TREATMENT WITH ASPIRIN) SHOWED (A): SLIGHT RECOVERY FROM SHRINKAGE (B): SLIGHT RECOVERY FROM DEGENERATED GLOMERULUS. (C): SLIGHT RECOVERY FROM DEGENERATED RENAL TUBULES. (D): SLIGHT RECOVERY FROM NECROTIC RENAL TUBULES

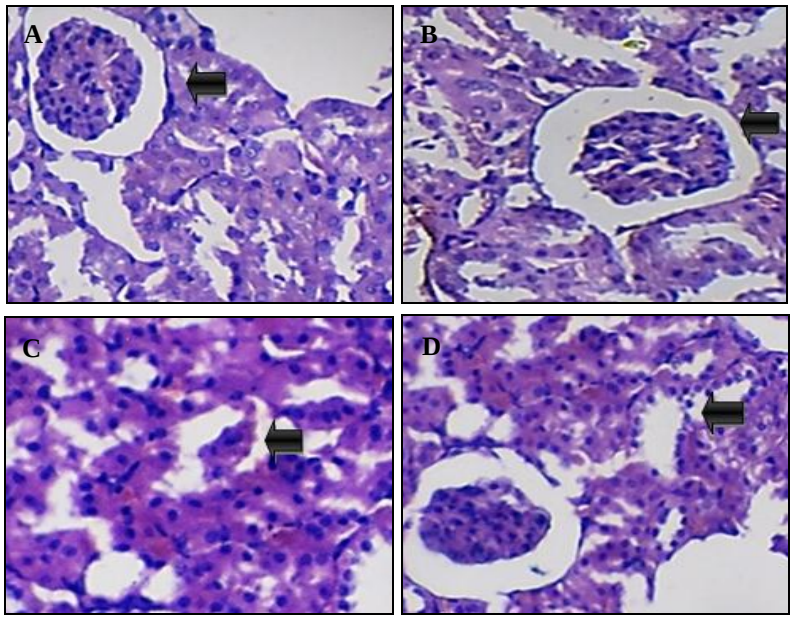

FIG. 6: PHOTOMICROGRAPH OF THE RAT KIDNEY SECTIONS (TREATMENT WITH CLOPIDOGERAL) SHOWED (A): MILD RECOVERY FROM SHRINKAGE (B): MILD RECOVERY FROM DEGENERATED GLOMERULUS. (C): MILD RECOVERY FROM DEGENERATED RENAL TUBULES. (D): MILD RECOVERY FROM NECROTIC RENAL TUBULES

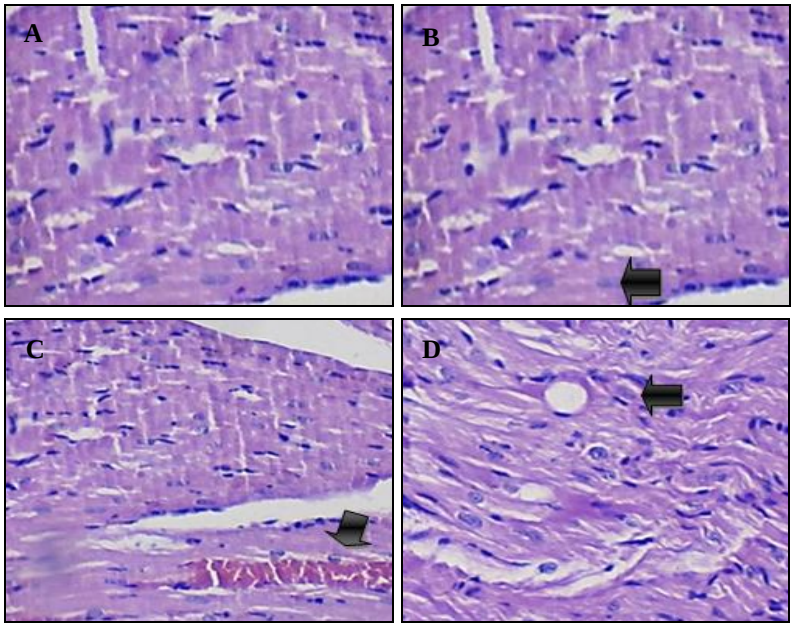

FIG. 7: PHOTOMICROGRAPH OF THE RAT HEART SECTIONS (OBESE RATS) SHOWED (A): NORMAL MYOCARDIUM. (B): HYPERTROPHOID MYOCARDIUM FIBERS (C): CONGESTION. (D): FATTY CHANGES

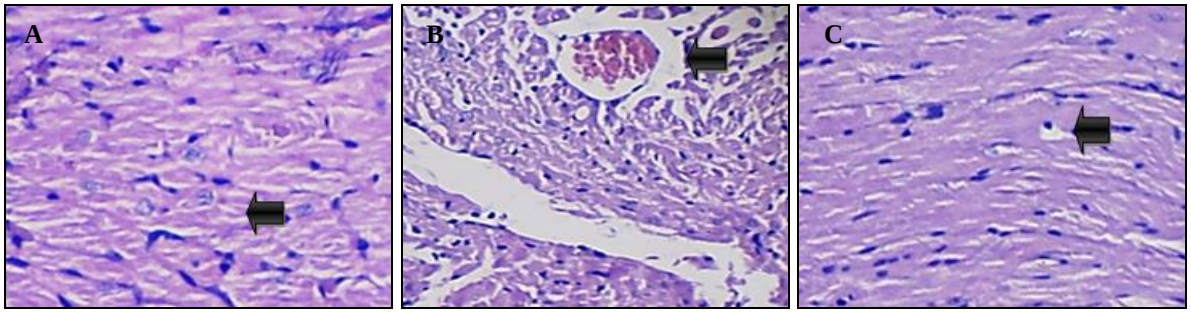

FIG. 8: PHOTOMICROGRAPH OF THE RAT HEART SECTIONS (TREATMENT WITH ASPIRIN) SHOWED (A): SLIGHT RECOVERY FROM HYPERTROPHOID MYOCARDIUM FIBERS (B): SLIGHT RECOVERY FROM CONGESTION. (C): SLIGHT RECOVERY FROM FATTY CHANGES

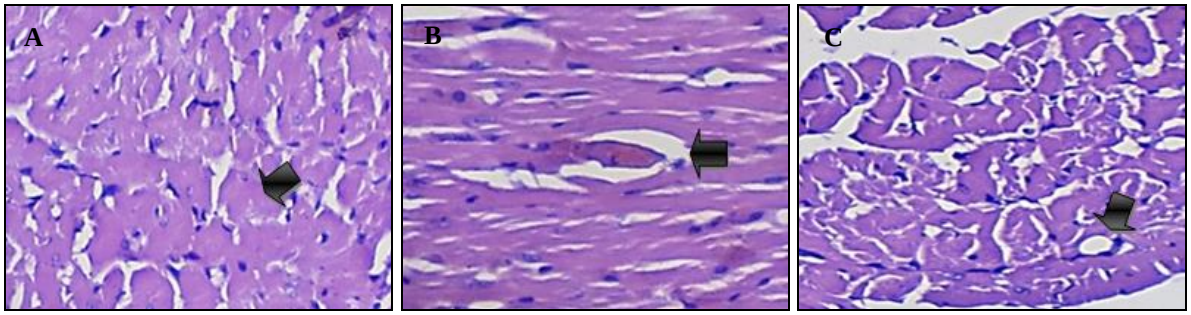

FIG. 9: PHOTOMICROGRAPH OF THE RAT HEART SECTIONS (TREATMENT WITH CLOPIDOGERAL) SHOWED (A): MILD RECOVERY FROM HYPERTROPHOID MYOCARDIUM FIBERS (B): MILD RECOVERY FROM CONGESTION. (C): MILD RECOVERY FROM FATTY CHANGES

DISCUSSION: Aspirin and clopidogrel are the preferred antiplatelets in the treatment of acute coronary syndrome as they block irreversibly TXA2 and ADP (P2Y12 subtype) that reduce platelet aggregation so that reduce acute coronary events [14]. The most frequent side effects of aspirin are dyspepsia and nausea. Patients should be counselled about the risk of bleeding, especially gastrointestinal (GI) bleeding, with aspirin [15]. Non-steroidal anti-inflammatory agents other than aspirin, as well as cyclooxygenase-2 (COX-2) selective anti - inflammatory agents, are contraindicated and should be discontinued at the time of ACS secondary to increased risk of death, reinfarction, HF, and myocardial rupture [16].

In the present study obesity was induced by allowing rats feed with beef tallow (90 g) and saturated fat (10 g), which contributed the majority of animal chow for 6 weeks [17]. Obesity has a direct relation to many diseases, including dyslipidemia, and CVS diseases. Obesity induced changes in lipoprotein metabolism and atherognic changes. The first step is elevated triglycerides; lipolysis of TG-rich lipoproteins are impaired in obesity by reduced mRNA expression levels of LPL in adipose tissue that will cause abnormalities in other lipoprotein metabolism [18, 19]. Studies using stable isotopes have shown a decreased catabolism of chylomicron remnants in obese subjects with the waist/hip ratio as the best predictor of the fractional catabolic rate [20].

However, Remnants of chylomicrons and VLDL are involved in the development of atherosclerosis [21]. Several investigators have demonstrated an association between TG-rich lipoproteins and remnant cholesterol levels with the presence of coronary [22], cerebral [23], and peripheral atherosclerosis. In addition to a direct detrimental effect by chylomicron remnants on vessels [24], impaired endothelial function after an oral fat load [25]. Other mechanisms of remnant-mediated atherogenesis, which may play a role in obesity, comprise the postprandial activation of leukocytes, generation of oxidative stress and production of cytokines [26]. Moreover, obesity may induce hyperglycemia through insulin resistance. The altered glucose homeostasis are caused by faulty signal transduction *via* the insulin signaling proteins, which results in decreased glucose uptake by the muscle, altered lipogenesis, and increased glucose output by the liver. The etiology of this derangement in insulin signaling is related to a chronic inflammatory state, leading to the induction of inducible nitric oxide syntheses and release of high levels of nitric oxide and reactive nitrogen species, which together cause posttranslational modifications in the signaling proteins [27].

However, in the present study, administration of antiplatelets, aspirin and clopidogrel to obese rats for seven days produced significant reduction in lipid profile and FBS. Many studies were supported our findings, Lou *et al*., 2016 found that low dose of aspirin or clopidogrel had a beneficial effect in reducing serum LDL cholesterol, Lp (a) and Hs-CRP levels and improve CHD [28, 29]. Platelets play a key role in atherogensis and thrombotic disorders. Platelet adhesion under conditions of high stress, as occurs in atherosclerotic arteries that have stenotic areas, is central to the development of arterial thrombosis; therefore, precise control of platelet adhesion must occur to maintain fluidity of blood and to prevent thrombotic or hemorrhagic complications [30].

The mechanisms underlying the proatherogenic function of platelets are increasingly well defined and involve specific adhesive interactions between platelets and endothelial cells at atherosclerotic-prone sites, leading to the enhanced recruitment and activation of leukocytes. Through the release of chemokines, proinflammatory molecules, and other biological response modulators, the interaction among platelets, endothelial cells, and leukocytes establishes a localized inflammatory response that accelerates atherosclerosis [31].

However, Aspirin and clopidogrel represent the cornerstone of treatment and secondary prevention of ischemic events in patients, including those with diabetes, presenting with either stable or unstable atherosclerotic cardiovascular disease [32]. Many studies showed that clopidogrel has benefits over aspirin; particularly in high-risk patients [33, 34, 35], all these findings supported the outcomes of the present study.

CONCLUSION: This study suggests that anti-platelet; particularly aspirin and clopidogrel were shown protective and dyslipidemic effects as they ameliorated obesity induced harmful effects on the rat's body including biochemical parameters and tissue damage. Clopidogrel findings showed slight beneficial effect than aspirin. Further studies are suggested to overcome the limitations of this work taking in consideration the clinical trial focusing on the duration and the sample size.

ACKNOWLEDGEMENT: The author would like to thank the Faculty of Pharmacy's graduated students, Jordan Medical Labs as well as the Pathologist Dr. Al Mansori A for their support to finish this work.

CONFLICT OF INTEREST: There is no conflict of interests regarding the publication of this paper.

REFERENCES:

1. Harikrishnan S, Leeder S, Huffman M, Jeemon P and Prabhakaran D: A Race against Time: The Challenge of Cardiovascular Disease in Developing Economies. 2nd ed. New Delhi, India: New Delhi Centre for Chronic Disease Control. Current Epidemiology and Future Directions 2014.
2. Klop B, Elte JWF and Cabezas MC: Dyslipidemia in Obesity: Mechanisms and Potential Targets. Nutrients 2013; 5(4): 1218-1240.
3. Grundy SM, Arai H and Barter P: An International Atherosclerosis Society position paper: global recommendations for the management of dyslipidemia: Executive summary. Atherosclerosis 2014; 232(2): 410-413.
4. Dordevic: Molecular basis of thrombophilia. J Med Biochem 2014; 33: 22-27.
5. Zehnder JL: Drugs Used in Disorders of Coagulation in Basic and Clinical Pharmacology. Katzung B, Masters S and Trevor A (eds). Mc Graw Hill 2014; 601-618.
6. Harvey RA: Blood drugs in Pharmacology Lippincott's Illustrated Review, Williams and Wilkins 2012; 5: 243-264.
7. Mainous AG, Tanner RJ, Shorr RI and Limacher MC: Use of aspirin for primary and secondary cardiovascular disease prevention in the United States, 2011-2012. J Am Heart Assoc 2014; 3(4).
8. Bath: Antiplatelet therapy with aspirin, clopidogrel, and dipyridamole versus clopidogrel alone or aspirin and dipyridamole in patients with acute cerebral. ischaemia (TARDIS): a randomised, open-label, phase 3 superiority trial. Radio Sciences 2017; S0140-6736(17): 32849-0.
9. Silva: Acute management of unstable angina and non-ST segment elevation myocardial infarction. einstein. 2015; 13(3): 454-61.
10. Fatemi MJ: The Effect of Enoxaparin and Clopidogrel on Survival Random Skin Flap in Rat Animal Model. World J Plast Surg 2012; 1(2): 64-70.
11. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). NIH Publication no 2001; 01-3670.
12. Stein EA and Myers GL: National Cholesterol Education Program Recommendations for Triglycerides Measurement: Executive Summary. Clin Chem 1995; 41: 1421-1426.
13. Knudson PE and Weinstock RS: Carbohydrates. In: Henry JB, ed. Clinical Diagnosis and Management by Laboratory Methods. Philadelphia: WB Saunders 2001; 20: 211-223.
14. Amsterdam EA, Wenger NK and Brindis RG: AHA/ACC Guideline for the management of patients with non-ST-elevation acute coronary syndromes: A report of the American College of Cardiology / American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; 64(24): e139-e228.
15. Bhatt DL, Hulot JS, Moliterno DJ and Harrington RA: Antiplatelet and anticoagulation therapy for acute coronary syndromes. Circ Res 2014; 114(12): 1929-1943.
16. O'Gara PT, Kushner FG and Ascheim DD: ACCF/ AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation / American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013; 61(4): e78-e140.
17. Reiser R, Sorrels MF and Williams MC: Influence of high levels of dietary fats and cholesterol on atherosclerosis and lipid distribution in swine. Circ Res 1959; 7: 833-846.
18. Blair HA and Dhillon S: Omega-3 carboxylic acids (epanova): A review of its use in patients with severe hypertriglyceridemia. Am. J. Cardiovasc. Drugs 2014.
19. Clemente-Postigo M, Queipo-Ortuno MI, Fernandez-Garcia D, Gomez-Huelgas R, Tinahones FJ and Cardona F: Adipose tissue gene expression of factors related to lipid processing in obesity. PLoS One 2011; 6: e24783.
20. Figueiredo: Fatty Acids Consumption: The Role Metabolic Aspects Involved in Obesity and Its Associated Disorders. Nutrients 2017; 9: 1158. doi:10.3390/nu9101158
21. Sanin V, Pfetsch V and Koenig W: Dyslipidemias and cardiovascular prevention: Tailoring treatment according to lipid phenotype. Curr. Cardiol. Rep 2017; 19: 61.
22. Jorgensen AB, Frikke-Schmidt R, West AS, Grande P, Nordestgaard BG and Tybjaerg-Hansen A: Genetically elevated non-fasting triglycerides and calculated remnant cholesterol as causal risk factors for myocardial infarction. Eur. Heart J 2012.
23. Banerjee and Chimowitz: Stroke Caused by Atherosclerosis of the Major Intracranial Arteries. Circulation Research 2017; 120: 502-513. Doi: 10.1161/CIRCRESAHA.116.308441
24. Klop B and Cabezas CM: Chylomicrons: A key biomarker and risk factor for cardiovascular disease and for the understanding of obesity. Curr. Cardiovasc. Risk. Rep 2012; 6: 27-34.
25. Abumrad NA and Davidson NO: Role of the gut in lipid homeostasis. Physiol. Rev 2012; 92: 1061-1085.
26. Lyons C, Kennedy E and Roche H: Metabolic inflammation-differential modulation by dietary constituents. Nutrients 2016; 8: 247.
27. Lauterbach and Wunderlich: Macrophage functions in obesity-induced inflammation and insulin resistance 2017; 469(3-4): 385-396
28. Lou G, Chen J and Xia Y: Effects of low-dose aspirin in subjects with dyslipidemia. Lipids Health Dis. 2016; 15: 106.
29. Levine GN, Bates ER and Bittl JA: ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology / American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2016; 68: 1082.
30. Wu: Platelets and von Willebrand factor in atherogenesis. Blood 2017; 129: 1415-1419. doi: https://doi.org/10.1182/blood-2016-07-692673
31. Coenen: Platelet interaction with activated endothelium: mechanistic insights from microfluidics. Blood 2017; 130: 2819-2828. doi:https://doi.org/10.1182/blood-2017-04-780825
32. Werf. FD: Prevention of Cardiovascular Events in Patients with Diabetes How Beneficial is Dual Antiplatelet Therapy? Circulation 2017; 135: 1675-1676.
33. Xian Y, Wang TY, McCoy LA, Effron MB, Henry TD, Bach RG, Zettler ME, Baker BA, Fonarow GC and Peterson ED: Association of discharge aspirin dose with outcomes after acute myocardial infarction: insights from the Treatment with ADP Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events after Acute Coronary Syndrome (TRANSLATE-ACS) Study. Circulation 2015; 132: 174-181.
34. Rollini F, Franchi F and Angiolillo DJ: Switching P2Y12-receptor inhibitors in patients with coronary artery disease. Nat Rev Cardiol 2016; 13: 11-27.
35. Bagai A, Peterson ED, Honeycutt E, Effron MB, Cohen DJ, Goodman SG, Anstrom KJ, Gupta A, Messenger JC

and Wang TY: In-hospital switching between adenosine diphosphate receptor inhibitors in patients with acute myocardial infarction treated with percutaneous coronary intervention: Insights into contemporary practice from the translate-ACS study. Eur Heart J Acute Cardiovasc Care 2015; 4: 499-508.

How to cite this article:
Ibrahim DA: Dyslipidemic and protective effects of aspirin and clopidogrel in obese rats. Int J Pharm Sci & Res 2018; 9(9): 3647-55. doi: 10.13040/IJPSR.0975-8232.9(9).3647-55.