

Impact of Parasterone Hormone on Heart Tissue in Female Rabbits with Induced Atherosclerosis

Ghfran Adnan Abdul Amir¹, Batool A. Hussein²

¹ Biology department, College of Education for pure sciences, University of Karbala, Iraq.

² Dr. A. Prof, Biology department, College of Education for pure sciences, University of Karbala, Iraq.

ABSTRACT

The use of laboratory animal models has greatly advanced the understanding of human diseases, particularly in basic research, drug development, and diagnostic tool creation. Among these, rabbits have been instrumental in studying human atherosclerosis due to their unique lipoprotein metabolism, which closely resembles that of humans and distinguishes them from rodent models. Rabbit models not only provide critical insights into the pathophysiology and progression of atherosclerosis but also play a pivotal role in translational research. Historically, rabbits were the first animal model used to study human atherosclerosis over a century ago. Currently, three main types of rabbit models are widely employed in atherosclerosis and lipid metabolism research: (1) cholesterol-fed rabbits, which simulate dietary-induced hypercholesterolemia; (2) heritable hyperlipidemic rabbits, which mimic human familial hypercholesterolemia due to genetic deficiencies in LDL receptors; and (3) genetically modified rabbits, including transgenic and knock-out models, engineered to investigate specific genetic factors involved in lipid metabolism and atherosclerosis. These models continue to provide invaluable contributions to understanding human cardiovascular disease and the development of novel therapeutic strategies.

Keywords: Parasteron, heart, cardiovascular disease, atherosclerosis

INTRODUCTION

In Western nations, atherosclerosis continues to be the primary cause of death for the elderly. Research suggests that with increasing age, inflammation and levels of endogenous sex hormones have an independent and increasing influence on the risk of atherosclerosis [1]. Although the precise effects of changes in endogenous sex hormone levels in women on atherosclerosis remain unclear, testosterone and estrogen are receiving more attention in research [2]. It is hypothesized to play a role in the cause, prevention, and treatment of atherosclerosis [3].

The mechanisms of the positive effect of progesterone on atherosclerosis in women are still not completely known. Arterial atherosclerosis is the main mechanism behind ischemic heart disease, although important (2020:13: A defect in the endothelial layer and micro vascular system can also cause ischemia, which is More common in women [4, 5]. Atherosclerosis occurs as a result of damage to blood vessels and their dysfunction, and is often caused by risk factors such as high blood pressure, diabetes, dyslipidemia, and smoking. This is followed by an inflammatory response that leads to plaque formation. In severe cases, plaque rupture and thrombosis can lead to Myocardial infarction (heart injury) [6]. Women seem to have higher rates of cardiovascular disease risk factors than males do, including high blood pressure, diabetes, and smoking. Compared to men, women who have these variables are more likely to have cardiovascular disease [4]. For instance, smoking has a relative risk that is doubled for men and ranges from -25 for women. Diabetes appears to be associated with an increased adjusted risk of fatal coronary artery disease in women as opposed to men in terms of cardiovascular disease (HR 14.7 (95% CI 6.2-35.3 3.8 vs. In the modern context, there is increasing evidence indicating that there are differences between the sexes in the characteristics of atherosclerotic plaque, as before menopause, it is noted that the incidence of coronary

heart disease in women is lower than in men in the same age group. However, it appears that after menopause, the incidence of heart disease increases in women than in men [7]. DHEA (Dehydroepiandrosterone) is a naturally produced hormone. It is converted into DHEA hormone in the body, and is secreted by the adrenal glands and sex glands. DHEA plays an important role in many other hormones in the body, including estrogen and testosterone. It plays an important role in Maintaining hormonal balance and the health of many organs and systems in the body Estrogen, a major female hormone, plays an important role in cardiovascular health, as estrogen enhances the synthesis of nitric oxide, a substance that helps blood arteries dilate and enhances blood flow. It lowers blood pressure. These hormones contribute to improving cholesterol levels in the blood, as estrogen increases cholesterol levels, and these hormones have an effect on (LDL) and reduce levels of harmful cholesterol (HDL). Good cholesterol is an anti-inflammatory that helps prevent blood vessel infections, and thus reduces the risk of heart diseases. These hormones encourage repair of blood vessels and reduce the accumulation of fatty plaques. Estrogen improves blood vessel function and reduces the possibility of clot formation. Compared to premenopausal women, postmenopausal women have a much greater incidence of cardiovascular illnesses, and it is believed that the incidence is linked to decreased ovarian function, especially decreased sensory hormones. Although studies of the biological role of this hormone are incomplete, the aim of the current study is to determine the effect of giving the hormone after the development of arteriosclerosis

MATERIAL AND METHODS

Twenty adult female rabbits with an average initial body weight of 2000 kg and 8 months of age were used. The study is conducted in the

animal house at the College of Education for Pure Sciences in winter. The animals are randomly classified in 4 group (G1, G2, G3, G4). Group one (G1) five female rabbits are water and regular food are given as appositve control group. Group two (G2) five female rabbits are oral dosed 1.5 mg/kg of cholesterol powder only [8]. Group three (G3) five female rabbits where intake only oral with nutrition 1.5 mg/kg of the body's weight cholesterol powder and hormone parasteron 2mg/kg . Group four (G4) five female rabbit where intake only orally with 2 mg/kg body weight parasteron hormone [9]. After six weeks, the animals were sacrificed for extraction heart to study the effect of the hormone parasteron on atherosclerosis, and blood samples were drawn to measure cholesterol levels by using a centrifuge to extract plasma to estimate the concentration of cholesterol in blood serum according to the Allian, 1974 method, the cholesterol concentration was calculated according to the equation below:

$$\text{Concentration mg/dl} = \frac{\text{sample} \times n}{\text{Standard}}$$

$N=200$ concentration of the standard solution; Sample =Optical absorbance of serum sample; Standard =Optical absorbance of standard solution

Results

The results of the current study point out the effect of cholesterol at a concentration of 1.5 mg/kg of the body weight for six weeks in the appeared of pathological changes in the wall of the aorta, represented by the appearance of acute infiltration in the wall with accumulation of fats in phagocytic cells, cells with the appearance of fatty streak and chronic inflammation compared to the healthy control group. Regarding the histopathological alterations in the heart of the cohort administered 1.5 mg/kg of cholesterol and 2 mg/kg of the hormone parasteron, an improvement in endothelial cells and a small accumulation of fat cells is observed, and no inflammation or congestion in the tissue. The treated group in parasteron The level of parasteron was increased in the heart of rabbits with atherosclerosis (Fig 1-8).

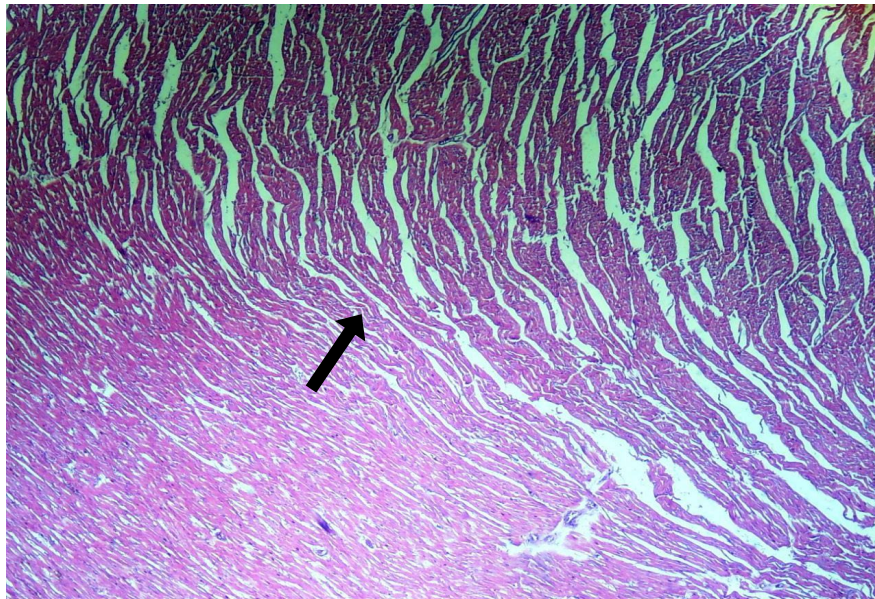


FIGURE 1: Histological Section of the Heart in a Group of Animals to Control where Normal Heart Muscles → (H&E10X)

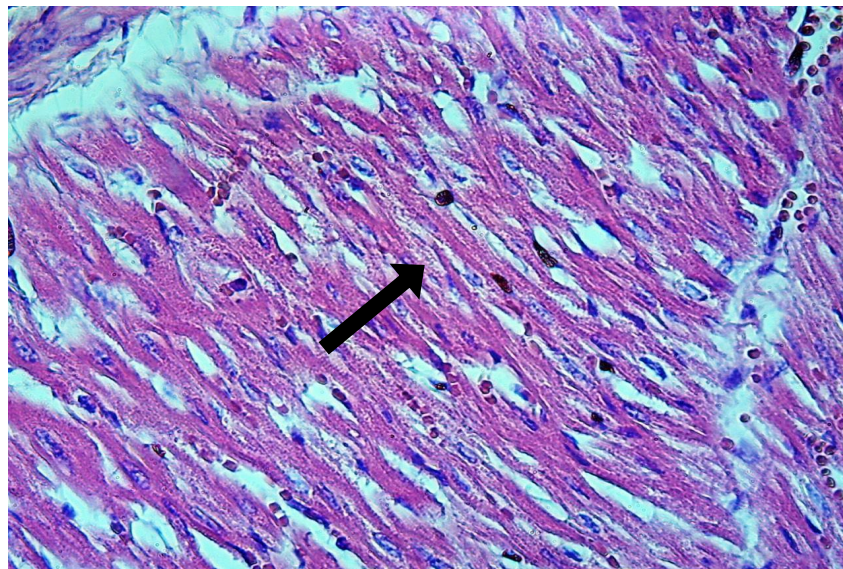


FIGURE 2: Show a Histological Section of the Heart in a Group of Animals where Normal Heart Muscles → (H&E40X)

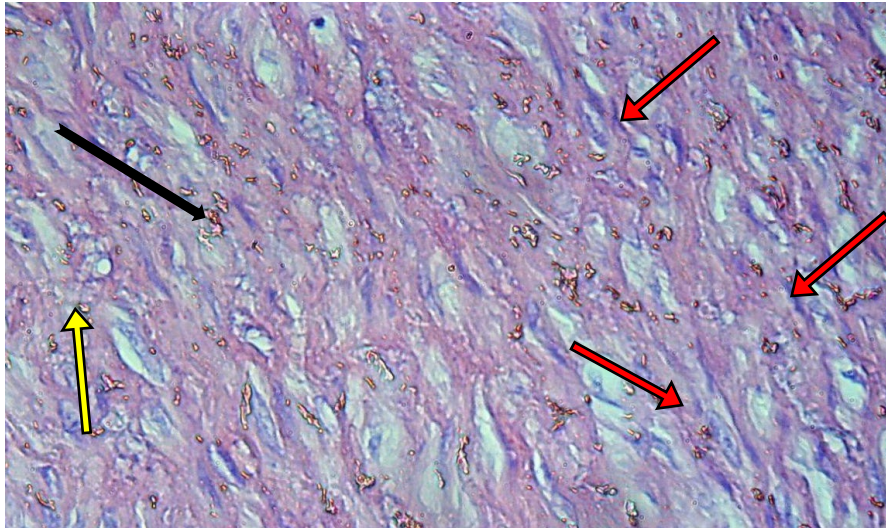


FIGURE 3: Histological Section of the Heart in a Group Of Animals Exposed to 1.5 mg/kg Cholesterol Diet, where Large Numbers of Foamy Cells Appear and the Tissue becomes Congestion and is Sent to Fatty Substances → (H&E40X)

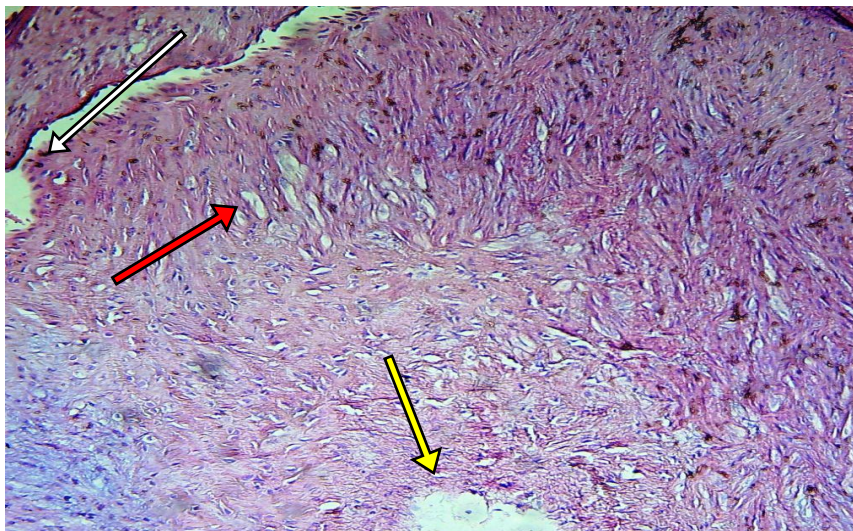


FIGURE 4: Histological Section of the Heart in a Group of Animals Exposed to 1.5 mg/kg Cholesterol Diet, where Large Numbers of Foamy Cells Appear and the Tissue Becomes Congestion and is Sent to Fatty Substances → (H&E10X)

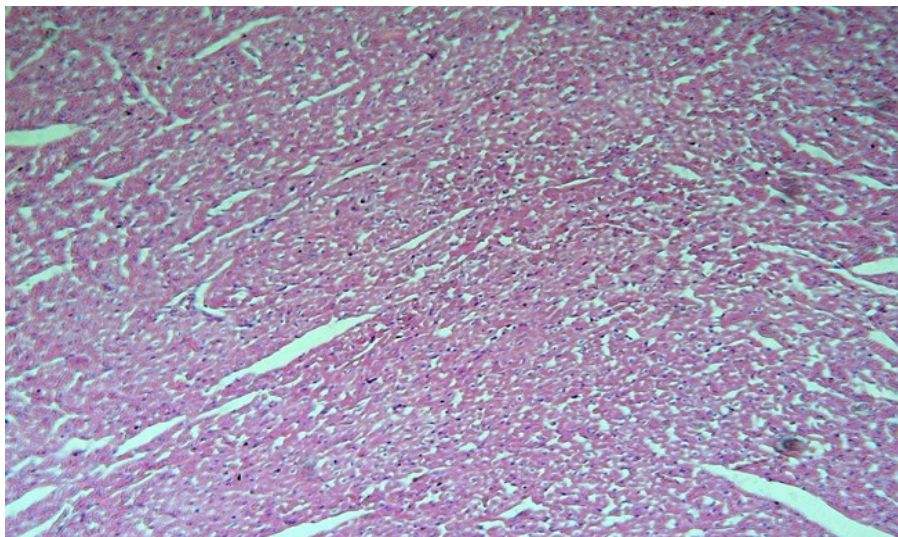


FIGURE 5: Heart Tissue Section in the Group of Animals Exposed to Cholesterol 1.5mg/kg and Parasteron Hormone 2mg/kg ,where the Appearance of fewer foamy cells and Tissue Congestion → (H&E 10X)

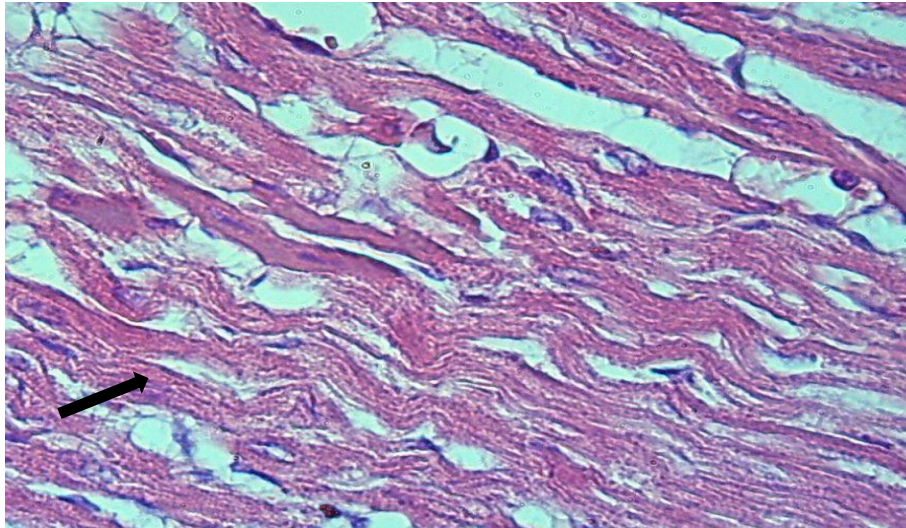


FIGURE 6: Heart Tissue Section in the Group of Animals Exposed to Cholesterol 1.5mg/kg and Parasterone Hormone 2mg/kg ,where the Appearance of Fewer Foamy Cells → and Tissue Congestion → (H&E 40x)

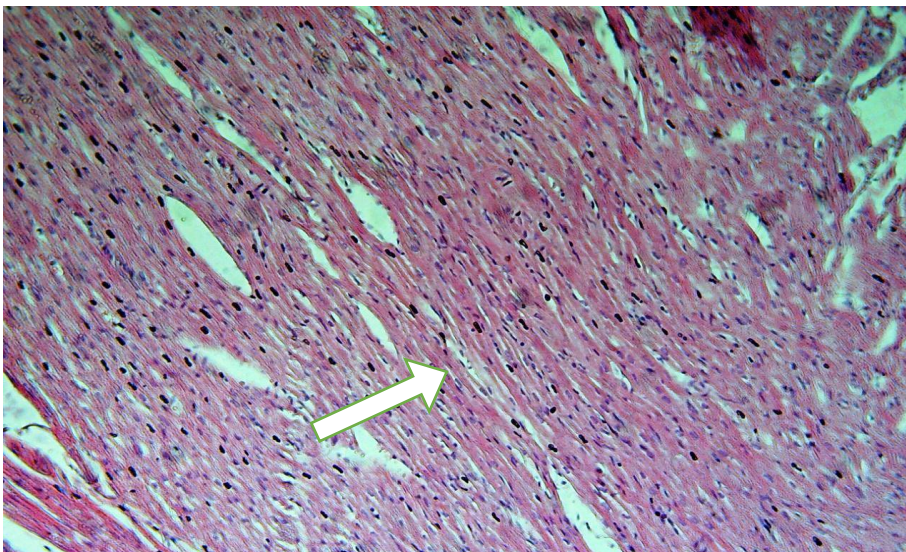


FIGURE 7: Histological Section in the Group of Animals Exposed to Parasterone where he Notices where a Rise is High Level of the Parasterone and Few Inflamentary Cells → with Focal Fibroses → (H&E10X)

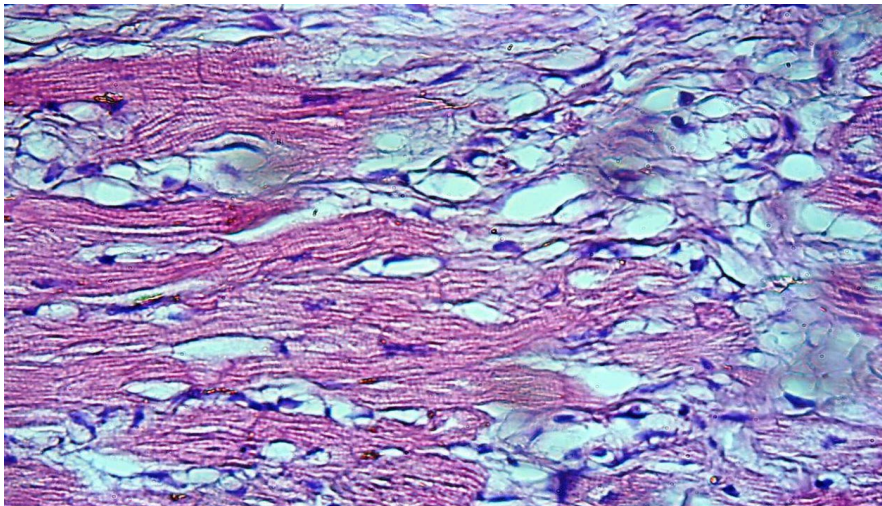


FIGURE 8: Histological Section in the Group of Animals Exposed to Parasterone where he Notices where a Rise is High Level of the Parasterone and Few Inflamentary Cells with Focal Fibroses → (H&E40X)

Discussion

Atherosclerosis is an enlargement defined by irregular plaques located within large and medium-sized arteries. The primary lesion is called pneumatic plaque, or fibrous plaque, and is mostly accumulating due to cholesterol and cholesterol esters (fats) that accumulate in its center. This cube is a fibrous patch, so its increase size affects the light of the arteries, which in turn affects its circumference. Initially, fibrous plaques are localized in specific locations of the periarterial artery, and as these plaques progress, they grow larger and occupy large extensions. With this advancement, you can close the arterial light and invade the submedia.5.

The prolonged use of cholesterol of 1.5 mg/kg for a period of six weeks leads to the occurrence of pathological changes in the lining of the heart, represented by necrosis of the tunica intima and peeling with the presence of vasculitis and degeneration and necrosis in the smooth muscle fibers and this is consistent with [10]. The damage of the inner lining of the artery is due to the particles of harmful lipoproteins is resulted from the treatment with cholesterol [11] which are oxidized through free radicals such as hydroxyl radicals, hydrogen peroxide or oxidation enzymes, as the oxidation of fats contributes significantly to the development of inflammation in the heart tissue and the formation of a lesion. Atherosclerosis through increased lipid oxidation in low-density lipoprotein particles, which leads to a change in membrane permeability and increased adhesion of white blood cells and platelets to the endothelial cells of the damaged heart, which in turn leads to increased inflammation and thus an increase in accusative cells to form foam cells that lead to a fatty chain. In the wall of the artery, which stimulates the proliferation and the migration of smooth muscle cells to the lining of the artery to increase the thickness and hardening of the deposits and the formation of a fibrous cover that

causes narrowing of the artery and thus the occurrence of cardiovascular diseases [12]. Due to a drop in antioxidant levels and a rise in effective oxygen species that oxidize fatty compounds, oxidative stress is a significant factor in the formation of atherosclerotic plaques. LDL-C generates ox-LDL, which support tissue damage through the production of large amounts of free radicals in a way that exceeds antioxidants, which are the catalyst for the process of atherosclerosis [13-15]. Since parasteron lowers the level of the inflammatory cytokine, it helps prevent cardiovascular disease. Numerous studies have proposed that the aging-related development of DHEA deficiencies could be a major factor in the etiology of numerous ailments, including cardiovascular abnormalities like atherosclerosis, and also play a vital part in the deterioration of many functions. The progression of carotid atherosclerosis. However, a favorable correlation has been documented between DHEAS levels and CVD outcomes in postmenopausal women (e.g., in the WISE Study Evaluating Ischemia Syndrome in Women). The better atherosclerotic status of individuals with greater DHEAS levels may have contributed to this [16, 17]. A number of physiological or pathophysiological conditions, including brain development, aging, osteoporosis, immune-mediated rheumatic diseases, diabetes-induced obesity, chronic heart failure (especially when linked to oxidative stress), and, more recently, vascular remodeling as it relates to pulmonary arterial hypertension, have been shown to benefit from DHEAS, according to other studies [14-16]. Where dhe acts as an adjunct enzyme.

Conclusion

The study in question points out that parasteron hormone helps partially to treat atherosclerosis by improving the inner lining of the heart. It is recommended that this hormone is used in relevant treatments.

References

- [1] N. D. Wong *et al.*, "Sex differences in coronary artery calcium and mortality from coronary heart disease, cardiovascular disease, and all causes in adults with diabetes: the coronary calcium consortium," *Diabetes Care*, vol. 43, no. 10, pp. 2597-2606, 2020.
- [2] L. J. Shaw *et al.*, "Sex differences in calcified plaque and long-term cardiovascular mortality: observations from the CAC Consortium," *European heart journal*, vol. 39, no. 41, pp. 3727-3735, 2018.
- [3] A. Mehta *et al.*, "Predictive value of coronary artery calcium score categories for coronary events versus strokes: impact of sex and race: MESA and DHS," *Circulation: Cardiovascular Imaging*, vol. 13, no. 8, p. e010153, 2020.
- [4] M. J. Budoff *et al.*, "Ten-year association of coronary artery calcium with atherosclerotic cardiovascular disease (ASCVD) events: the multi-ethnic study of atherosclerosis (MESA)," *European heart journal*, vol. 39, no. 25, pp. 2401-2408, 2018.
- [5] A. A. Kelkar *et al.*, "Long-term prognosis after coronary artery calcium scoring among low-intermediate risk women and men," *Circulation: Cardiovascular Imaging*, vol. 9, no. 4, p. e003742, 2016.
- [6] R. Nakanishi *et al.*, "All-cause mortality by age and gender based on coronary artery calcium scores," *European Heart Journal—Cardiovascular Imaging*, vol. 17, no. 11, pp. 1305-1314, 2016.
- [7] D. Skuratovskaia, M. Vulf, A. Komar, E. Kirienkova, and L. Litvinova, "Promising directions in atherosclerosis treatment based on epigenetic regulation using microRNAs and long noncoding RNAs," *Biomolecules*, vol. 9, no. 6, p. 226, 2019.
- [8] M. Setorki, S. Asgary, and B. Nazari, "Reduces Cholesterol induced atherosclerotic lesion in aorta hyper cholesterolemic rabbits," *J medicinal plant Research*, vol. 5, no. 9, pp. 1518-1525, 2011.
- [9] M. Obaid, "Physiological role of Dehydroepiandrosterone (DHEA) on pituitary-Adrenal—Ovarian Axis in Adult Female Rats Msc," Thesis. College of Veterinary Medicine, University of Baghdad, 2016.
- [10] S. S. Virani *et al.*, "Heart disease and stroke statistics—2020 update: a report from the American Heart Association," *Circulation*, vol. 141, no. 9, pp. e139-e596, 2020.
- [11] D. Zhao *et al.*, "Endogenous sex hormones and incident cardiovascular disease in post-menopausal women," *Journal of the American College of Cardiology*, vol. 71, no. 22, pp. 2555-2566, 2018.
- [12] W. Xue, Y. Deng, Y.-F. Wang, and A.-J. Sun, "Effect of half-dose and standard-dose conjugated equine estrogens combined with natural progesterone or dydrogesterone on components of metabolic syndrome in healthy postmenopausal women: a randomized controlled trial," *Chinese medical journal*, vol. 129, no. 23, pp. 2773-2779, 2016.
- [13] V. M. Miller *et al.*, "The Kronos early estrogen prevention study (KEEPS): what have we learned?," *Menopause*, vol. 26, no. 9, pp. 1071-1084, 2019.
- [14] D. Pérez-Cremades, A. Mompeón, X. Vidal-Gómez, C. Hermenegildo, and S. Novella, "miRNA as a new regulatory mechanism of estrogen vascular action," *International Journal of Molecular Sciences*, vol. 19, no. 2, p. 473, 2018.

- [15] K. Husain, W. Hernandez, R. A. Ansari, and L. Ferder, "Inflammation, oxidative stress and renin angiotensin system in atherosclerosis," *World journal of biological chemistry*; vol. 6, no. 3, p. 209, 2015.
- [16] T. F. Lüscher, "An update on heart failure and peripheral arterial disease," *European heart journal*, vol. 36, no. 15, pp. 885-887, 2015.
- [17] T. Wongwarawipat, N. Papageorgiou, D. Bertsias, G. Siasos, and D. Tousoulis, "Olive oil-related anti-inflammatory effects on atherosclerosis: potential clinical implications," *Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders)*, vol. 18, no. 1, pp. 51-62, 2018.



This is an open-access article distributed under the terms of the Creative Commons Attribution License.