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Comparative Histopathological Effects of Semaglutide and Liraglutide on the liver, kidney, and abdominal aorta in High-Fat- Induce Obese Male Albino Rats

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I. Abstract

Semaglutide and liraglutide are glucagon-like peptide-1 (GLP-1)–based diabetes drugs. Semaglutide possesses a longer half-life. Utilizing relatively lower doses. Then the aim of the study is to compare the beneficial metabolic effects of these 2 drugs in rats fed a high-fat diet (HFD), aiming to deepen our mechanistic understanding of their energy homeostatic functions. This study used 30 albino male rats, obtained from the animal house of the College of Veterinary Medicine, Tikrit University, from January 1, 2025, to March 21, 2025. The experiment was divided into six groups: Group 1 (G1): Control group that received the standard diet throughout the experiment. Group 2 (G2): Fattened control group that received the special diet throughout the experiment. Group 3 (G3): obese rats with low doses of semaglutide (0.5 mg/kg). Group 4 (G4): obese rats with high doses of semaglutide (1.0 mg/kg). Group 5 (G5): obese rats with low doses of liraglutide (0.2 mg/kg). Group 6 (G6): obese rats with high doses of liraglutide (0.4 mg/kg). The present study indicated that semaglutide and liraglutide have a protective and histological effect against the pathological changes associated with obesity, with a relative superiority of higher doses in reducing inflammatory damage and cellular degeneration and improving the microstructure of the studied organs.

Keywords: Obesity, semaglutide, liraglutide, histological study

II. Introduction

Obesity is complex and chronic condition characterized by excessive accumulation of body fat to an extent that impairs normal physiological condition and adversely affect health. It is commonly assessed using body mass index which is calculated as body weight in kilograms divided by the square of height in meters (kg/m^2), and is widely used to classify individuals as overweight or obese (1, 2). Overweight and obesity are risk factors for type 2 diabetes, making their management a critical public health priority (3, 4). In addition to medication-based weight loss, lifestyle modifications, such as diet and exercise, are currently advised for the treatment of obesity(5).

Among these therapies, glucagon_like peptide receptor (GLP-1R) agonist have gained considerable attention due to their metabolic benefit. Semaglutide is an antidiabetic drug, which mitigates blood glucose via stimulating Semaglutide along acting GLP_1 receptor agonist, is widely used as an antidiabetic agent that Improve glycemic control by enhancing insulin secretion and suppressing glucagon release(6). Semaglutide possesses multiple clinical benefits, including significant weight reduction, blood pressure lowering, and cardio protection (7). Experimental studies have also highlighted the potential organ-protective effects of semaglutide. For instance, Reis-Barbosa et al. documented hepatoprotective effects of semaglutide in a study conducted on obese mice via

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suppression of the mTOR pathway and stimulation of insulin signaling together with the AMPK pathway. Furthermore, another animal study demonstrated the nephroprotective effect of semaglutide. The author stated that semaglutide improved the albuminuria and attenuated the severity of glomerulosclerosis (8).

Furthermore, GLP-1 receptor agonists has been associated improved in lipid metabolism and reduction of oxidative stress which may contribute to protecting the glomerular barrier and preventing the progression of kidney damage in models of obesity and diabetes (9).

Another widely used GLP-1 receptor agonist is liraglutide, which shares similar mechanisms of action with semaglutide but differs in pharmacokinetic properties and duration of action. Liraglutide enhances insulin secretion, suppresses glucagon release, and delays gastric emptying, thereby contributing to improved glycemic control and weight reduction(10). However, despite the therapeutic similarities between semaglutide and liraglutide, differences in their molecular structure and pharmacodynamics may result in variable biological and histopathological effects. To date, limited studies have directly compared their impact on organ histology under experimental conditions. Therefore, this study aimed to investigate the effect of the semaglutide and liraglutide, on histopathological section of the liver, kidney, and abdominal aorta in an experimental animal model.

Methodology

Studies Animals

This study used 30 albino male rats, weighing between 170 and 200 gm, obtained from the animal house of the College of Veterinary Medicine, Tikrit University. The rats were placed in plastic cages and reared for 80 days, from January 1, 2025, to March 21, 2025, at the animal house of the College of Veterinary Medicine, Tikrit University. The rats were kept under suitable environmental conditions, including ventilation, a temperature of 25°C, and 12 hours of light. The cages were lined with wood shavings, and the animals were left for two weeks before the start of the experiment to settle in and adapt to their environment.

Drug Doses & Method of Adminstration

Rybelsus tablets containing 14 mg of semaglutide were obtained from a local pharmacy. The product was manufactured by Novo Nordisk (Denmark). The tablets were used after being prepared according to the experimental protocol for oral administration. Semaglutide was administered on a daily basis throughout the experimental period.

Similarly, Saxenda (liraglutide) was obtained from a local pharmacy and manufactured by Novo Nordisk (Denmark). It was supplied as a prefilled injectable formulation and administered via subcutaneous injection at the specified doses in the study design. liraglutide was injected once weekly.

The experiment was divided into two phases:

Phase 1 (Fattening Phase):

This phase lasted from week 0 to week 6, during which all experimental animals (except the control group) were fed a high-fat diet to induce obesity. The control group (G1) received a standard diet throughout this period.

Phase Two (Treatment)

This phase began after week 6. During this phase, the rats were treated with the aforementioned drugs. The rats in the second group continued to be fed the special diet, while the control group and the remaining groups were fed the standard diet. The groups were divided into six animals each, as follows:

•Group 1 (G1): Control group that received the standard diet throughout the experiment

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•Group 2 (G2): Fattened control group that received the special diet throughout the experiment
•Group 3 (G3): Fattened rats + low doses of semaglutide (0.5 mg/kg) (11)
•Group 4 (G4): Fattened rats + high doses of semaglutide(1.0 mg/kg) (11)
•Group 5 (G5): Fattened rats + low doses of liraglutide(0.2 mg/kg) (12)
•Group 6 (G6): Fattened rats + high doses of liraglutide(0.4 mg/kg) (12)

Preparation of Microscopic Slides

The rats were anesthetized with chloroform and then dissected. The organs of interest (liver, kidney, and abdominal aorta) were carefully excised and immediately rinsed in 0.9% physiological saline solution (NaCl) to remove blood and adherent debris. Subsequently, the tissues were transferred into 10% neutral buffered formalin for fixation for 24–48 hours prior to histological processing.

III. Result

Histological examination of the abdominal aorta in the control group (G1) revealed a normal vascular architecture (Figure 1). The tunica intima was lined by a single layer of simple squamous endothelial cells resting on an intact basement membrane. The tunica media consisted of regularly arranged elastic lamellae interspersed with smooth muscle cells, while the tunica adventitia contained loose connective tissue. The aortic lumen was filled with normal blood components.

ln contrast, the obese control group (G2) exhibited marked histopathological alterations (Figure2), including endothelial cell disruption, fragmentation of elastic lamellae. disorganization of smooth muscle cells, and the vacuolation of smooth muscle cells were also evident.

Treatment with semaglutide resulted in dose-dependent improvement. In the low-dose semaglutide group (G3) partial restoration of endothelial integrity was observed, with relatively organized elastic lamellae and reduced degenerative changes (Figure3). The high-dose semaglutide group (G4) demonstrated near-normal aortic architecture, characterized by well-organized elastic fibers, intact endothelial lining. and minimal inflammatory changes (Figure4)

Similarly, liraglutide treatment improved aortic histology. The low-dose liraglutide group(G5) showed partial restoration of vascular structure with residual mild endothelial disruption and limited smooth muscle degeneration (Figure5). The high-dose liraglutide group (G6) exhibited significant recovery. with improved organization of elastic lamellae and smooth muscle cells, although mild loosening of connective tissue in the tunica media was still observed (Figure6).

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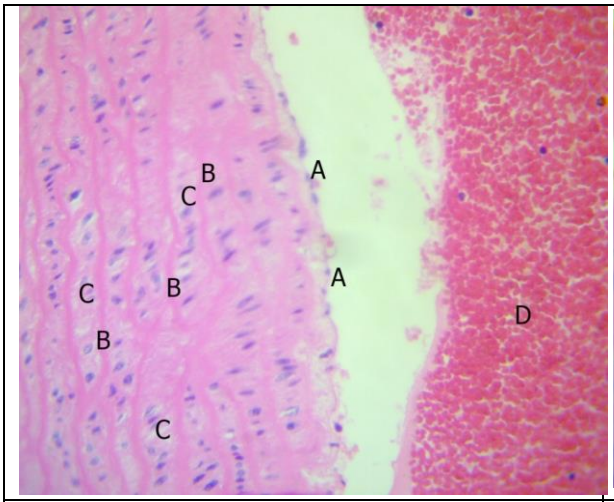

Figure (1) Histological section of the aorta from the control group showing the aortic wall and containing the tunica intima (A), tunica media (B), tunica externa (C), blood clot in the aortic lumen (D): (H&E X10)

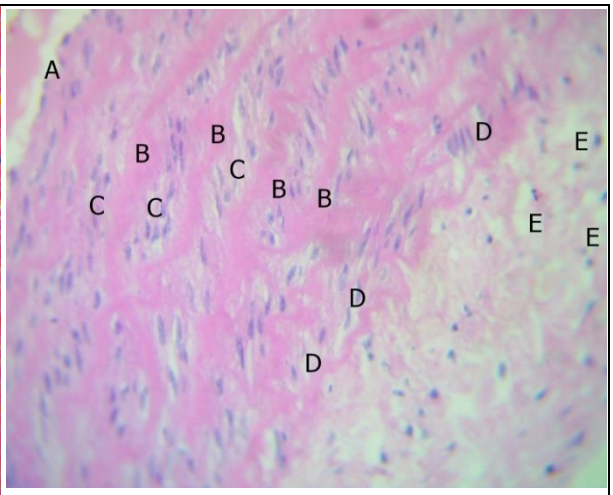

Figure (2) Histological section of the aorta of the obese group, endothelial cells (A) elastic laminae (B) mass of smooth muscle cells (C) cytoplasmic rupture of some muscle fibers (D) pigment-free fatty droplets (E)

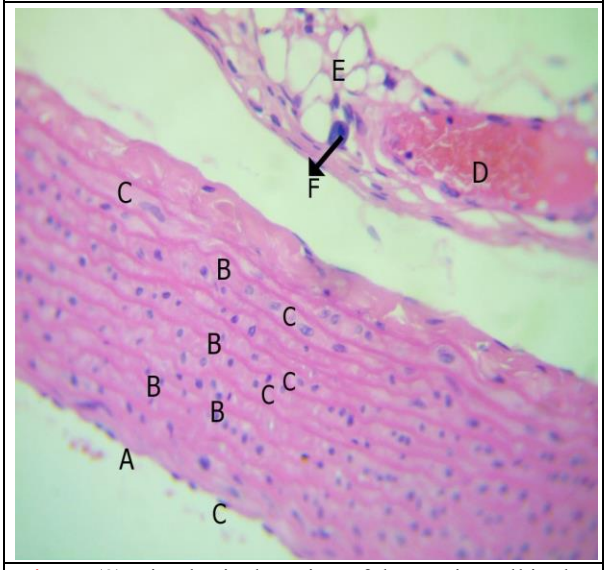

Figure (3) Histological section of the aortic wall in the third group treated with a low concentration of semaglutide, tunica intima with endothelial cells attached to the basement membrane (A) tunica media with elastic lamellae (B) rows of smooth muscle cells (C) tunica adventitia with a blood vessel congested with blood (D) adipose tissue (E) macrophages (F)

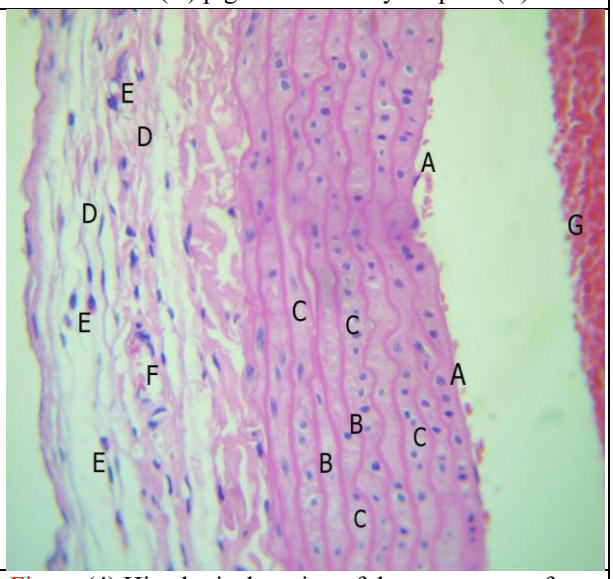

Figure (4) Histological section of the aorta, group four, treated with a high concentration of semaglutide. The tunica intima, containing squamous cells (A), the tunica media, containing elastic laminae parallel to each other (B), smooth muscle cells (C), the tunica adventitia, containing loose colloid connective tissue (D), white blood cells and phagocytes (E), blood capillaries (F), blood in the aortic lumen (G).

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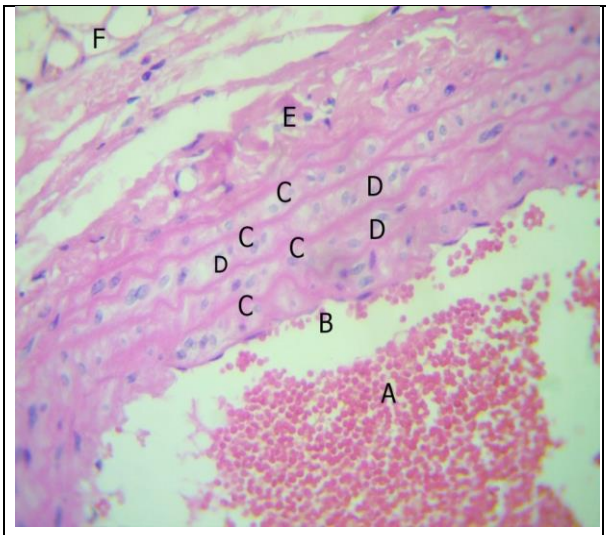

Figure (5) Histological section of the aorta in the fifth group treated with a low concentration of liraglutide, hematoma in the aortic lumen (A) tunica intima (B) tunica media containing elastic laminae (C) smooth muscle fibers (D) necrosis of some muscle cells in the outer part of the tunica media (E) fatty tissue in the tunica adductae (F)

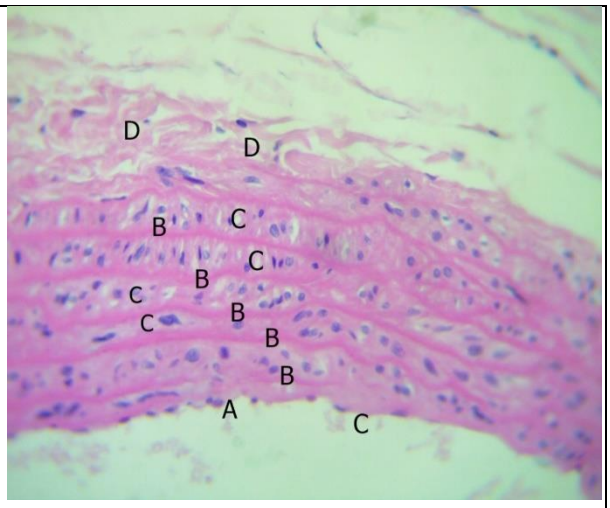

Figure (6) Histological section of the inner tunica albuginea of the aorta in the sixth group treated with a high concentration of liraglutide, containing endothelial cells (A) The middle tunica albuginea, containing elastic laminae (B) Smooth muscle fiber clusters, containing large, dark-colored nuclei (C) Glucofibrous clusters of the outer tunica albuginea (D)

Histological examination of the kidney in the control group (G1) revealed a normal cortical and medullary architecture (Figure7). The renal cortex showed well-formed glomeruli surrounded by Bowman's capsule and a clear capsular space. proximal convoluted tubules were lined with columnar epithelial cells and had narrow lumina, while distal convoluted tubules were lined with simple cuboidal epithelium and exhibited wider lumina. The renal medulla showed normal tubular organization without pathological changes.

In contrast. the obese control group (G2) demonstrated marked histopathological alterations (Figure8) including glomerular inflammation vascular congestion thickening of renal arterial walls and leukocyte infiltration tubular necrosis the medulla showed interstitial inflammation epithelial shedding and marked vascular congestion

Treatment with semaglutide induced dose-dependent improvement the low-dose semaglutide group (G3) showed partial restoration of renal architecture (Figure9) with near-normal glomerular morphology reduced inflammatory infiltration and partial preservation of tubular structure although mild fibrin deposition and epithelial shedding persisted

In the high-dose semaglutide group (G4) further improvement was observed (Figure10) characterized by better-preserved glomeruli reduced interstitial inflammation and near-normal appearance of medullary tubules only mild residual epithelial degeneration and vascular congestion were noted

Similarly, liraglutide treatment improved renal histology. The low-dose liraglutide group(G5) exhibited partial recovery of glomerular structure with localized capsular space dilation mild inflammatory infiltration and limited

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tubular epithelial detachment (Figure 11). The high-dose liraglutide group (G6) showed substantial recovery, with near-normal glomerular and tubular architecture. reduced inflammation. and improved vascular integrity, although mild fibrin strands were still observed in some tubules (Figure12).

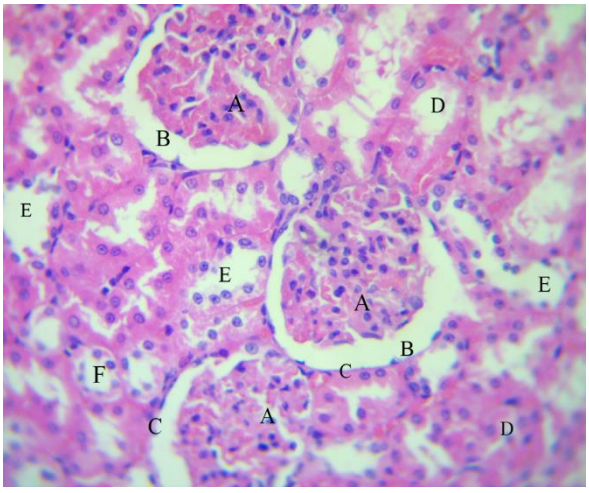

Figure (7) Histological section of the renal cortex, control group, semi-lobular renal glomeruli (A), capsular space (B), Bowman's capsule (C), proximal coiled tubules (D), distal coiled tubules (E), loop of Henle (F) (H&E X40)

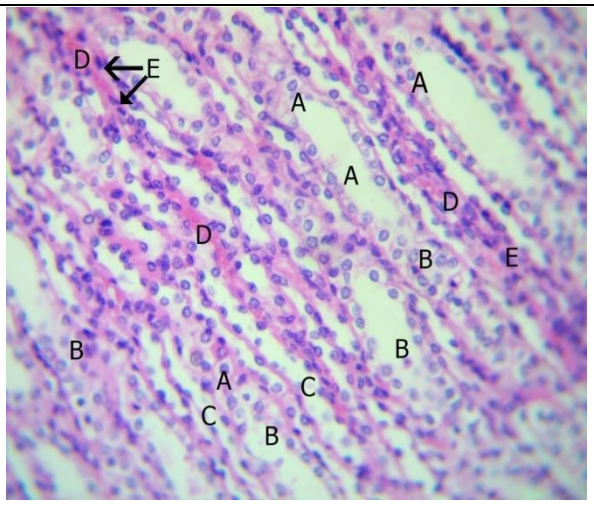

Figure (8) The kidney medulla, the obese group, the renal tubules lined with hypertrophic cuboidal cells with cytoplasmic rupture (A) Shedding of epithelial cells in the tubular lumen (B) Thin terraces of the loop of Henle (C) Blood congestion between the tubules (D) White blood cells with phagocytes (E)

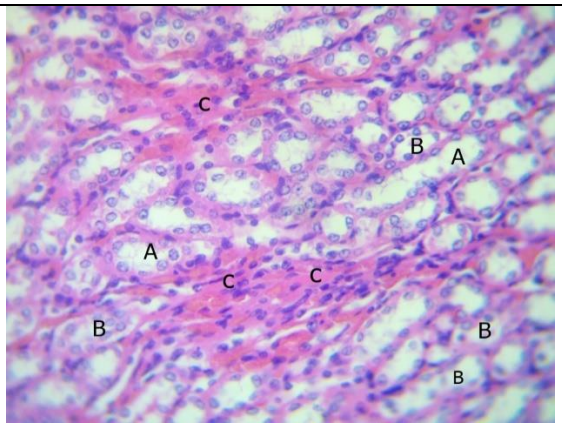

Figure (9) Histological section of the kidney medulla of the third group treated with a low concentration of semaglutide, renal tubules lined with simple cuboidal cells (A) Cellular detachment in the lumen of some tubules (B) Hematogenous congestion and lysis of the capillaries of the interstitial tissue (C)

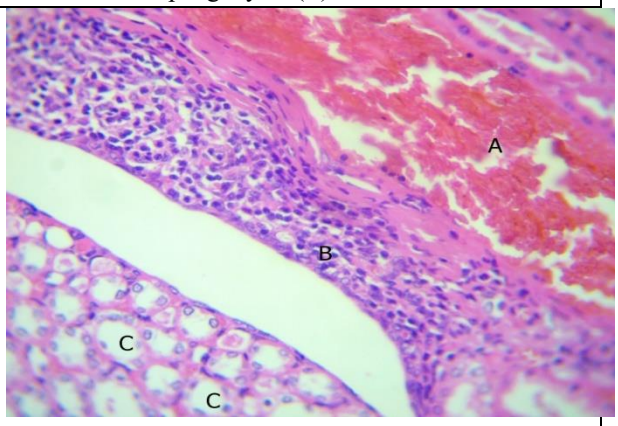

Figure (10) Histological section of the kidney medulla in the fourth group treated with a high concentration of semaglutide, acute congestion of the renal vein (A), massive infiltration of white blood cells (B), normal-shaped renal tubules (C).

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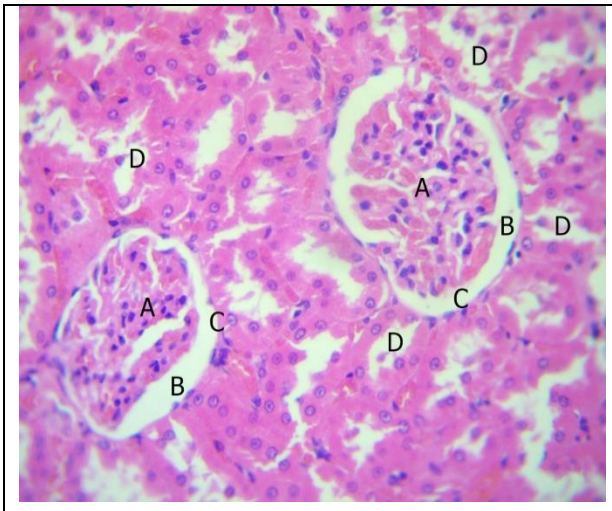

Figure (11) Histological section of renal glomeruli that are semi-lobed and have white blood cells on their surface (A) Enlargement of the capsular space (B) Bowman's capsule (C) Epithelial shed in the lumen of coiled tubules (D) Hemorrhage (E)

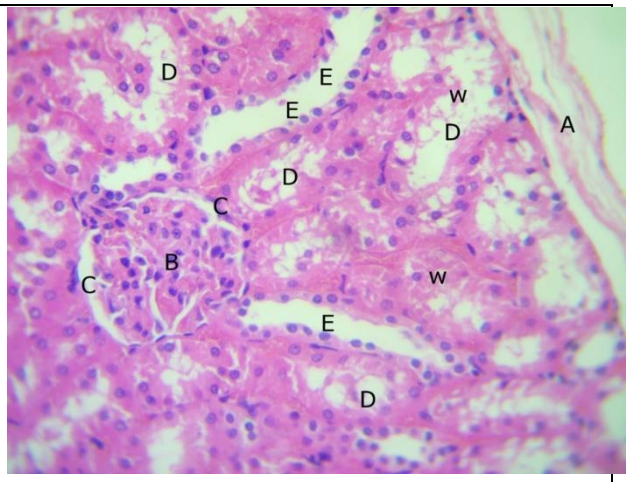

Figure (12) Histological section of renal capsule composed of loose colloidal fibers (A) Normally shaped renal glomerulus (B) Bowman's capsule (C) Fibrils in the tubular lumen (D) Normally shaped distal coiled tubules (E) Decomposition in cell walls (W)

Histological examination of the liver in the control group (G1) revealed normal hepatic architecture (Figur13). The hepatic lobules sowed a well -preserved structure with a central vein surrounded by radiating cords of hepatocytes. Hepatocytes appeared polygonal with eosinophilic cytoplasm and centrally located round nuclei, blood sinusoids were clearly visible and contained kupffer cells without evidence of pathological changes.

In contrast the obese control group(G2) exhibited marked histopathological alterations (Figur14) including hepatocellular degeneration, fatty changes (hepatic steatosis), sinusoidal congestion and focal inflammatory cell infiltration. The presence of lipid vacuoles within hepatocytes and vascular congestion indicated significant hepatic injury induced by obesity.

Treatment with simaglutide resulted in dose- dependent improvement. The low-dose semaglutide group G3 showed partial restoration of hepatic structure (Figure15) with reduced lipid accumulation and improved hepatocyte morphology, however, mild inflammatory infiltration and vascular congestion were still present. In the high-dose semaglutide group G4 liver architecture appeared close to normal (Figure16) with well-organized hepatocyte cords reduced steatosis and minimal inflammatory cell infiltration, although mild portal inflammation was still observed

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Similarly, liraglutide treatment improved hepatic histology. The low-dose liraglutide group (G5) demonstrated partial recovery with reduced steatosis and moderate restoration of hepatocyte structure, although mild inflammatory infiltration and sinusoidal dilation persisted (Figure 17). The high-dose liraglutide group (G6) showed marked improvement (Figure 18), characterized by nearly normal hepatic lobular architecture, reduced lipid deposition, and improved sinusoidal organization, although mild portal inflammatory infiltration was still present.

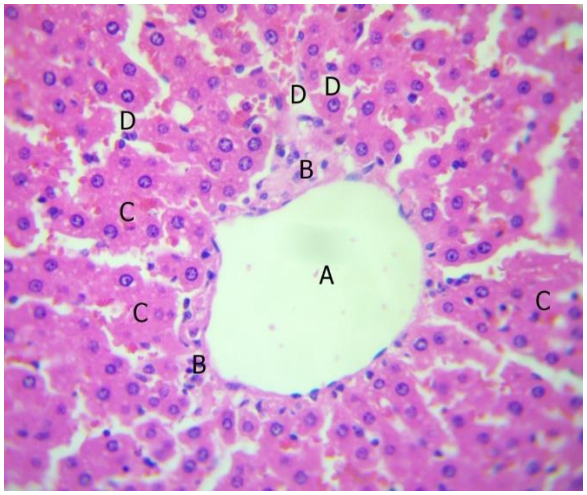

Figure (13) The liver lobe, the central vein is free of blood (A) Infiltration of white blood cells around the vein wall (B) Rows of hepatocytes with dark spherical nuclei (C) Reticulum of hematopoiesis with Cowper cells (D) and red blood cells (H&E X40)

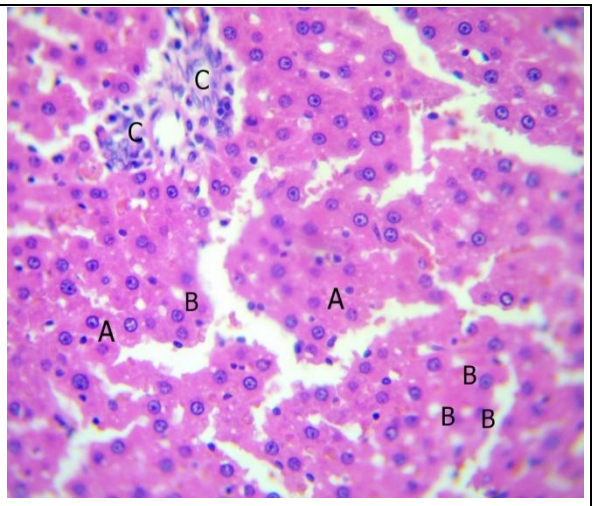

Figure (14) Section of liver tissue, fat group, hepatocyte clusters (A) Fat droplets in the cytoplasm of some hepatocytes (B) Focal infiltration of white blood cells (C)

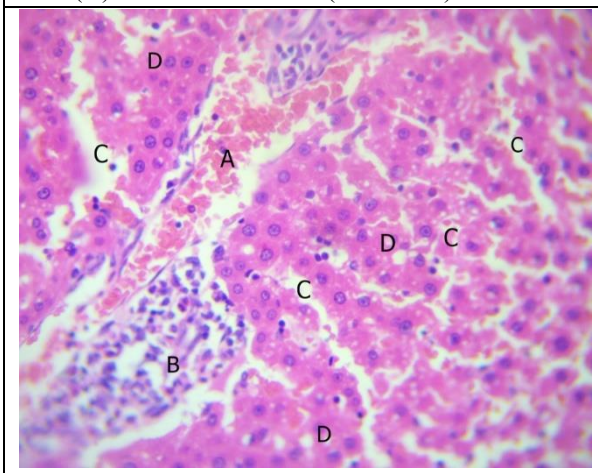

Figure (15) Histological section of the liver in the third group treated with a low concentration of semaglutide, central vein containing red and white blood cells (A) nodular lymphatic infiltration around the vein wall (B) blood sinuses containing red blood

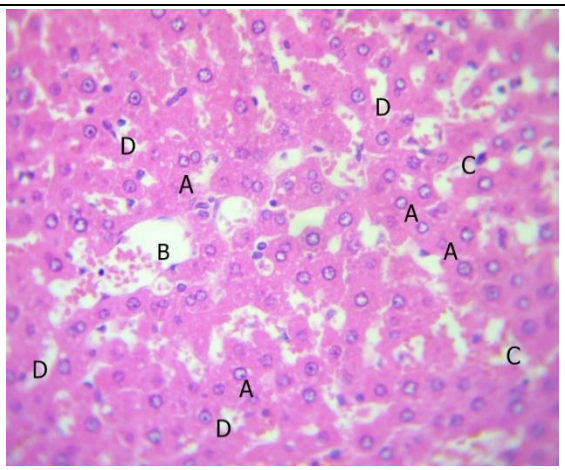

Figure (16) Liver tissue in the fourth group treated with a high concentration of semaglutide, rows of liver cells with spherical nuclei, pale staining (A) enlargement of some blood sinuses containing red blood cells (B) Coover cells (C) blood sinuses (D)

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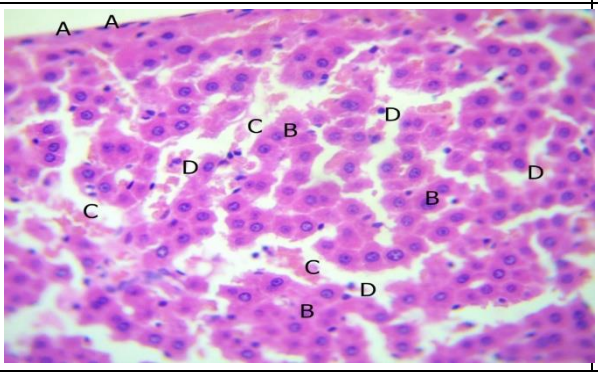
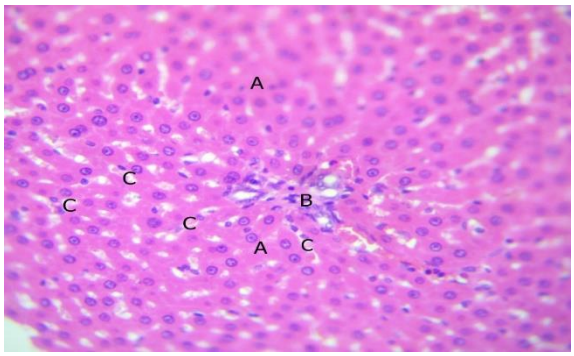
cells and Cowper cells (C) clusters of liver cells containing fine fat droplets (D)	
	
Figure(17) The thin liver capsule (A) Polygonal clusters of hepatocytes with dark-stained spherical nuclei (B) Wide-lubrilized sinusoidal network containing red blood cells (C) Coover cells (D)	Figure (18) Histological section of the liver in the hour group treated with a high concentration of liraglutidee drug, showing hepatocyte hyperplasia (A), focal lymphocytic infiltration around the hepatocytes (B), blood sinuses containing Coover cells (C).

Discussion

Histopathological findings in the present study demonstrated that obesity induced marked structural alterations in the abdominal aorta, kidney, and liver, characterized by vascular thickening, inflammatory infiltration, and tissue degeneration. This study demonstrated that semaglutide exhibited superior histopathological effects compared to liraglutide in the aorta, liver, and kidney, showing greater improvement in tissue architecture and overall organ protection. These findings are consistent with those of (13), who demonstrated increased vessel thickness and edema of endothelial cells in the aorta of obese rats, along with pyknosis, detachment from the inner elastic membrane, and loss of intercellular junctions .These changes in vascular characteristics in obese rats suggest that semaglutide has the potential to improve aortic function and address structural changes associated with obesity. A study by (13) demonstrated that liraglutide's protective effect on the aorta is not associated with increased insulin levels or endogenous GLP-1 secretion, confirming that its direct mechanism of action relies on modulating the inflammatory response of aortic endothelial and smooth muscle cells, rather than on its anti-diabetic and anti-obesity effects.

Both semaglutide and liraglutide reduce mesothelial thickness and vascular stiffness in animal models of obesity and atherosclerosis, and this is associated with improved endothelial cell function and reduced cellular inflammation and oxidative stress (14, 15). The results demonstrate that obesity causes renal damage characterized by glomerular and tubular changes, tissue inflammation, and vascular congestion. GLP-1 receptor agonists, on the other hand, contribute to reducing these changes to varying degrees depending on the concentration used. Both semaglutide and liraglutidee treatments were associated with reduced inflammation, improved lipid metabolism, and decreased oxidative stress, all of which positively impact glomerular and tubular cell integrity. The study's findings are consistent with (16), who indicated that semaglutide intervention can reduce glomerular and renal tubular damage by altering renal protein expression in mice. Glomerulopathy is the primary pathological manifestation of obesity-related kidney disease, resulting from fat accumulation in the kidneys. This accumulation

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causes oxidative stress and activates inflammatory processes, leading to damage to podocytes, which are the primary driving force behind the progression of obesity-related nephropathy (17).

Liraclotide has an approximate half-life of 12 hours in humans, while simaglutide has a longer half-life of approximately one week. Semaglutide is a modification of liraclotide at position 8 of the amino chain and leads to a significant reduction in HbA1c and body weight(18). When comparing high doses of both simaglutide and liraclotide, both drugs significantly improved renal structure. However, semaglutide was relatively more effective in reducing tubular changes and interstitial inflammation, while liraclotide exhibited a more profound effect on regulating the glomerular structures themselves. This differentiation may reflect the different molecular mechanisms of action of each drug, despite belonging to the same pharmacological class. Some studies suggest that semaglutide has longer-lasting effects compared to liraclotide due to its longer half-life and broader metabolic effects (19).

The study results were consistent with (20), who demonstrated semaglutide significant ability to improve pathological changes in hepatocytes, including edema and lymphocytosis, and to reduce fat accumulation in the liver. In the HFD group, significant collagen deposition was observed, while semaglutide exhibited clear antifibrotic activity, significantly reducing collagen surface area .Previous studies have shown that fatty acids and their metabolites are detrimental factors in the development of metabolically impaired fatty liver disease. The physiological mechanisms of this disease include increased fatty acid accumulation and decreased mitochondrial fatty acid oxidation, leading to impaired lipid metabolism in hepatocytes and fat accumulation. Additionally, hepatocyte injury resulting from TNF-α activation and the stimulation of free radical production (21). Under normal physiological conditions, the synthesis and breakdown of free fatty acids, triglycerides, and total cholesterol in the body are in a state of dynamic equilibrium. Hepatic steatosis occurs due to impaired fat accumulation in the liver, resulting from lipolysis in visceral adipose tissue, new hepatic lipid synthesis, increased consumption of a high-calorie, high-fat diet, and decreased β-mitochondrial oxidation in the liver. Ultimately, this leads to increased production and accumulation of plasma free fatty acids, and triglycerides (22).

Conclusion

Semaglutide and liraglutide have a protective and histological effect against the pathological changes associated with obesity, with a relative superiority of higher doses in reducing inflammatory damage and cellular degeneration and improving the microstructure of the studied organs.

IV. References

1. Yu J, Lee J, Lee S-H, Cho J-H, Kim H-S. A study on weight loss cause as per the side effect of liraglutide. Cardiovascular Therapeutics. 2022;2022(1):5201684.https://doi.org/10.1155/2022/5201684Digital

2. Reis-Barbosa PH, Marcondes-de-Castro IA, de Souza Marinho T, Aguila MB, Mandarim-de-Lacerda CA. The mTORC1/AMPK pathway plays a role in the beneficial effects of semaglutide (GLP-1 receptor agonist) on the liver of obese mice. Clinics and Research in Hepatology and Gastroenterology. 2022;46(6):101922.https://doi.org/10.1016/j.clinre.2022.101922

3. Wadden TA, Hollander P, Klein S, Niswender K, Woo V, Hale P, et al. Weight maintenance and additional weight loss with liraglutide after low-calorie-diet-induced weight loss: the SCALE Maintenance randomized study. International journal of obesity. 2013;37(11):1443-51

ISSN Onlin:2708 -9347, ISSN Print: 2708 -9339 Volume 15, Issue 1 (2026)

https://iasj.rdd.edu.iq/journals/journal/issue/20226 *https://doi.org/10.54174/utjagr.v13ii 432.*

4. Sarma S, Sockalingam S, Dash S. Obesity as a multisystem disease: Trends in obesity rates and obesity-related complications. Diabetes, Obesity and Metabolism. 2021;23:3-16.https://doi.org/10.1111/dom.14290Digital

5. Younossi ZM, Corey KE, Lim JK. AGA clinical practice update on lifestyle modification using diet and exercise to achieve weight loss in the management of nonalcoholic fatty liver disease: expert review. Gastroenterology. 2021;160(3):912-8

6. Smits MM, Van Raalte DH. Safety of semaglutide. Frontiers in endocrinology. 2021;12:645563.10.3389/fendo.2021.645563

7. Doggrell SA. Sgemaglutide in type 2 diabetes–is it the best glucagon-like peptide 1 receptor agonist (GLP-1R agonist)? Expert Opinion on Drug Metabolism & Toxicology. 2018;14(3):371-7.https://doi.org/10.1080/17425255.2018.1441286

8. Dalbøge LS, Christensen M, Madsen MR, Secher T, Endlich N, Drenic' V, et al. Nephroprotective effects of semaglutide as mono-and combination treatment with lisinopril in a mouse model of hypertension-accelerated diabetic kidney disease. Biomedicines. 2022;10(7):1661.https://doi.org/10.3390/biomedicines10071661

9. Abdelrahman AM, Awad AS, Hasan I, Abdel-Rahman EM. Glucagon-like peptide-1 receptor agonists and diabetic kidney disease: from bench to bed-side. Journal of Clinical Medicine. 2024;13(24):7732

10. Liu QK. Mechanisms of action and therapeutic applications of GLP-1 and dual GIP/GLP-1 receptor agonists. Frontiers in endocrinology. 2024;15:1431292

11. Weiskirchen R, Lonardo A. Semaglutide from Bench to Bedside: The Experimental Journey Towards a Transformative Therapy for Diabetes, Obesity and Metabolic Liver Disorders. Medical Sciences. 2025;13(4):265

12. Ivanov AN, Lagutina DD, Saveleva MS, Popyhova EB, Stepanova TV, Savkina AA, et al. Effect of liraglutide on microcirculation in rat model with absolute insulin deficiency. Microvascular Research. 2021;138:104206.https://doi.org/10.1016/j.mvr.2021.104206

13. Zhang K, Li R, Matniyaz Y, Yu R, Pan J, Liu W, et al. Liraglutide attenuates angiotensin II-induced aortic dissection and aortic aneurysm via inhibiting M1 macrophage polarization in APOE-/-mice. Biochemical Pharmacology. 2024;223:116170.https://doi.org/10.1016/j.bcp.2024.116170

14. Rakipovski G, Rolin B, Nøhr J, Klewe I, Frederiksen KS, Augustin R, et al. The GLP-1 analogs liraglutide and semaglutide reduce atherosclerosis in ApoE−/− and LDLr−/− mice by a mechanism that includes inflammatory pathways. JACC: Basic to Translational Science. 2018;3(6):844-57

15. Gaspari T, Welungoda I, Widdop RE, Simpson RW, Dear AE. The GLP-1 receptor agonist liraglutide inhibits progression of vascular disease via effects on atherogenesis, plaque stability and endothelial function in an ApoE−/− mouse model. Diabetes and Vascular Disease Research. 2013;10(4):353-60

16. Wang S, Zhang M, Yang X, Chen S. Protective Effect of Semaglutide on Obesity-Induced Renal Disease and Obesity-Induced Kidney Renal Clear Cell Carcinoma. Diabetes, Metabolic Syndrome and Obesity. 2025;https://doi.org/10.2147/DMSO.S498447:805-18.https://doi.org/10.2147/DMSO.S498447

17. Guo H, Wang B, Li H, Ling L, Niu J, Gu Y. Glucagon-like peptide-1 analog prevents obesity-related glomerulopathy by inhibiting excessive autophagy in podocytes. American Journal of Physiology-Renal Physiology. 2018;314(2):F181-F9.https://doi.org/10.1152/ajprenal.00302.2017

18. Zhou JY, Poudel A, Welchko R, Mekala N, Chandramani-Shivalingappa P, Rosca MG, et al. Liraglutide improves insulin sensitivity in high fat diet induced diabetic mice through multiple pathways. European journal of pharmacology. 2019;861:172594

19. Karimi MA, Gholami Chahkand MS, Dadkhah PA, Sheikhzadeh F, Yaghoubi S, Esmaeilpour Moallem F, et al. Comparative effectiveness of semaglutide versus liraglutide, dulaglutide or tirzepatide: a systematic review and meta-analysis. Frontiers in Pharmacology. 2025;16:1438318.https://doi.org/10.3389/fphar.2025.1438318

ISSN Onlin:2708 -9347, ISSN Print: 2708 -9339 Volume 15, Issue 1 (2026)

https://iasj.rdd.edu.iq/journals/journal/issue/20226 *https://doi.org/10.54174/utjagr.v13ii 432.*

20. Niu S, Chen S, Chen X, Ren Q, Yue L, Pan X, et al. Semaglutide ameliorates metabolism and hepatic outcomes in an NAFLD mouse model. Frontiers in Endocrinology. 2022;13:1046130.10.3389/fendo.2022.1046130

21. Berlanga A, Guiu-Jurado E, Porras JA, Auguet T. Molecular pathways in non-alcoholic fatty liver disease. Clinical and experimental gastroenterology. 2014:221-39

22. Friedman SL, Neuschwander-Tetri BA, Rinella M, Sanyal AJ. Mechanisms of NAFLD development and therapeutic strategies. Nature medicine. 2018;24(7):908-22