Original Article

Comparative Evaluation of Renal Tissue Changes Associated with Anti-Obesity Therapies: Hoodia Gordonii Extract, Liraglutide (Saxenda), and Their Combination

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ABSTRACT

Objective: To assess the histopathological effects of Hoodia gordonii extract and Saxenda as well as the effect of the combination on renal tissue under experimental conditions that simulated the effect of metabolic stress associated with obesity.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the University of Kufa, Iraq from 11th September 2024 to 28th February 2025.

Methods: This study was conducted to examine the effects Hoodia gordonii extract (150 mg/kg/day), Saxenda (0.1 mL/day, subcutaneous) and a combination of both on renal effects were investigated using experimental models over 30 and 45 days. Kidney specimens were fixed in 10% neutral buffered formalin and then sectioned and stained with Hematoxylin and Eosin (H&E) and observed under the microscope to determine glomerular and tubular changes.

Results: Samples exposed to Hoodia gordonii exhibited intact renal architecture that was not affected by glomerular or tubular injury. Saxenda exposure on the other hand caused histological alterations which included interstitial inflammation, tubular necrosis and glomerular enlargement. The joint regimen showed better morphology of the kidneys, almost normal histological characteristics and less damage.

Conclusion: Hoodia gordonii seems a safe natural adjunct in obesity control, and it shows a protective effect against the nephrotoxicity of the drug.

Key Words: Hoodia gordonii, Saxenda; obesity, Nephrotoxicity, Renal protection, Histopathology, Oxidative stress

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INTRODUCTION

Obesity has emerged as one of the most enduring nutritional and societal challenges of the contemporary age, especially in industrialized countries. It is defined by a pathological increase of adipose tissue because of an excessive number of fat cells, which is usually expressed by the body mass index (BMI), with a BMI of 30 kg/m 2 or more indicating obesity.

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The rising cases of obesity are much linked to the upsurge in chronic health-related diseases, including cardiovascular diseases, type 2 diabetes, some cancers and early deaths.[1,2]

Pathogenesis of obesity has a multifactorial nature, consisting of a complex of inherited predisposition, environmental factors, behavioral, and hormonal dysregulation, in addition to which recent studies have also introduced the significance of adipose tissue as a significant endocrine gland contributing to the overall chronic low-grade inflammation and metabolic complications associated with insulin resistance and lipid abnormalities.[3-5] The COVID-19 pandemic has also increased the rates of obesity, particularly in the most industrialized nations, including the United States, which has also.[6]

The existing anti-obesity interventions include lifestyle, surgical, pharmacologic and dietary supplements. The pharmacological agents are used to reduce appetite, prevent nutrient absorption or increase energy consumption. Although many drug candidates have been developed, it is unclear whether many of them will be safe and effective in the long term and few of them are approved by the regulatory authorities.[7,8]

A glucagon-like peptide-1 (GLP-1) receptor agonist has become the drug of interest, namely liraglutide (Saxenda), as it induces satiety and gastric emptying, as well as improves the metabolic parameters. Even though it shows encouraging weight loss effects, there are side effects like gastrointestinal discomfort and possible risks to other vital bodily organs such as kidneys and pancreas and hence the need to do some research on it.[9,10]

In line with the development of pharmacology, herbal remedies to control obesity have shown an increasing trend all over the world. Hoodia gordonii is a succulent plant that is indigenous to Southern Africa and has been used naturally as an appetite suppressant by indigenous people. The plant is a source of bioactive compounds including pregnane glycosides, including well-known P57 molecule which has been linked to appetite suppressive activity and metabolic control in preclinical models.[11-13]

Nonetheless, there are the ongoing worries as to the systemic safety of the synthetic and natural anti-obesity agents specifically, the absence of adequately-conducted clinical trials of Hoodia gordonii and the emerging cases of organ-specific toxicity when using liraglutide are subject to serious safety concerns. The histopathological examination is a useful model to measure tissue-level modifications caused by such interventions, especially in those organs vulnerable to drug toxicity, e.g. the liver, kidney, pancreas and heart.[14]

METHODS

The current experimental study was carried out in University of Kufa, Iraq between 11th September 2024 and 28th February 2025 under letter No. 37967 dated 5-10-2024. Thirty-two healthy adults, who were experiment subjects, were used and taken through a two-week acclimatization period prior to the start of an experiment. The experimental groups were randomly assigned eight samples (n = 8 per group) to test the histological effects of various doses of Hoodia gordonii extract, Saxenda (liraglutide) and the combination of the two at two time intervals, 30 and 45 days. These samples were randomly split into eight experimental groups (n = 8 each group) which were aimed at testing the histological effects of varying doses of Hoodia gordonii extract and Saxenda (liraglutide) and Hoodia gordonii extract combined with Saxenda (liraglutide): at two time points; 30 and 45 days. All the subjects were kept to the standard laboratory conditions at controlled temperatures of 22ff 1oC, relative humidity was kept at 5560 and 12-hour light dark cycle. Standard diet and water were given ad libitum, with exceptions made when the samplers were on a fast. All the procedures carried out in the laboratory were done in line with experimental ethical standards as well as the National institute of health (NIH) guidelines on the treatment and utilization of the laboratory models. The procedure of dosing was done through oral gavage (extract) and subcutaneous injection (Saxenda), with the specific dilutions being made every day in fresh solutions.

Authenticated Hoodia gordonii powder was supplied by Farm Vredelus PTY LTD, Douglas, Namibia, accompanied by a Certificate of Analysis and LC-MS chemical profiling. For extract preparation, 20 g of dry powder was soaked overnight in 100 ml of a dichloromethane–methanol solution (1:1), following the method by Corley and Miller. (2009). The extract was separated via centrifugation (3000 ×g for 15 minutes), pooled, and evaporated at 40°C. The final yield was 8% w/w of the original dry mass.

All the subjects were seeded and starved overnight before the treatment period of the 30 and 45 days were complete. Kidney samples were immediately washed in cold saline after which the samples were immobilized in 10 percent neutral buffered formalin (NBF) with a ratio of tissue to fixative of 1:10 and left to incubate with freshly prepared fixative.

After fixation, the tissues were dehydrated using ethanol graded (70, 80, 90, 95 and 100 percent) cleared in xylene and embedded in molten paraffin wax. Embedding The treatment involved using stainless steel moulds to orient the correct tissue then cooled in order to create paraffin blocks.

Paraffin blocks were sectioned into thin slices of 4-5 m thick with the help of a rotary microtome. The sections were then floated in a water bath at 40 to 45 degrees Celsius and put on adhesive covered glass slides and left there to dry overnight at 37 degrees Celsius.

Standard Hematoxylin and Eosin (H&E) staining was performed using the following sequence:

- Deparaffinization: Xylene (2 changes, 5 minutes each)
- Rehydration: Descending ethanol series (100% to 70%) → distilled water
- Staining: Hematoxylin (3–5 minutes) → tap water rinse → differentiation (acid alcohol) → bluing (alkaline water)
- Counterstaining: Eosin (1–2 minutes)
- Dehydration and clearing: Ascending ethanol → xylene
- Mounting: DPX mounting medium with coverslip

A light microscope was used to examine prepared slides at different magnifications. (40×, 100×, 400×) to assess:

- Cell morphology
- Tissue architecture
- Signs of degeneration, necrosis, inflammation, congestion, or fibrosis
- Comparative histological damage scores

RESULTS

The histological examination of the kidney tissue of the control group revealed that the tissue had normal renal

structure, intact nephrons and tubules. Similarly, the exposure of 30 and 45 days of the samples to the hot aqueous extract of the Hoodia gordonii seeds at 100mg/kg showed no histopathological variation hence the preservation of the renal structure use. On the other hand, kidney samples of subjects treated with Saxenda 0.1mg/kg, 30 and 45 days revealed varied changes of pathology, including tubular degeneration and glomeruli atrophy. However, preventive groups which were co-administered with Hoodia gordonii extract and the Saxenda also exhibited a normal or nearly normal kidney structure, suggesting that the plant extract was preventive (Figs. 1-2).

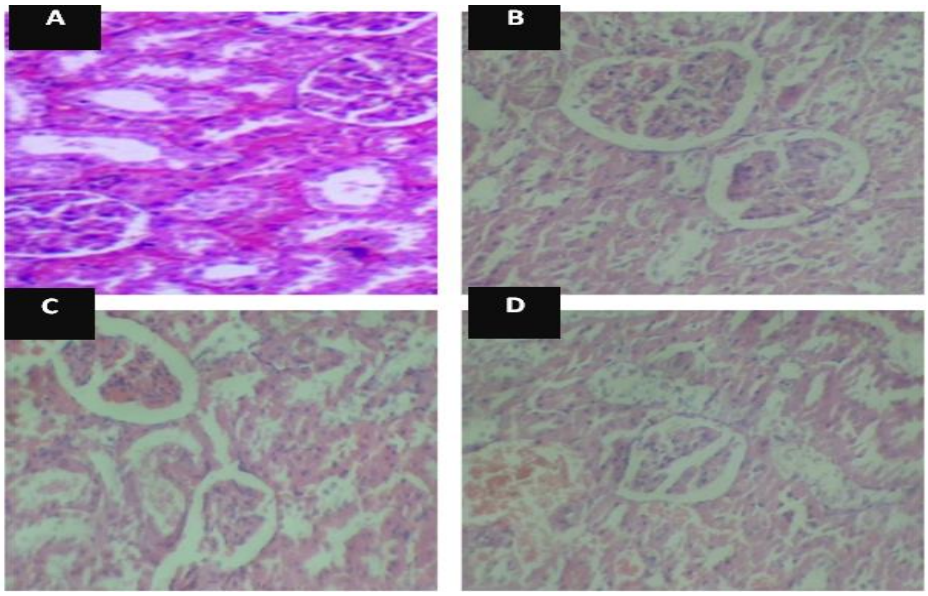

Figure No. 1: A normal kidney tissue control group. B: group treated with the aqueous extract of Hoodia at 150 mg/kg .C: group treated with the drug (0.1) mg/kg for 30 days. D: group that received treatment for 30 days with 150 mg/kg of Hoodia aqueous extract plus 0.1 mg/kg of the medication

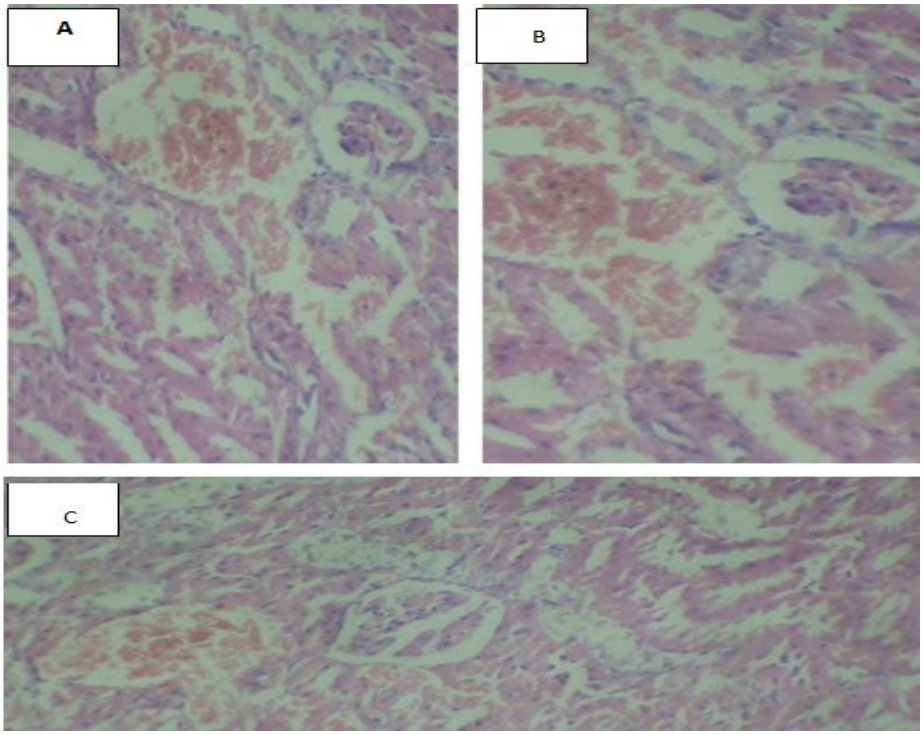

Figure No. 2: A: section of kidney of a sample of the group that was tested with Hoodia at concentration of 150mg, B: group treated with the drug (0.1)mg/kg over 45 days. C: A kidney belonging to a male rat of the group that was treated with an aqueous extract of hoodia at a concentration of 150 mg/kg + the drug at a concentration of (1.0)mg/kg in 45 days

DISCUSSION

The current research compared the results of renal histology of chronic administration of Hoodia gordonii extract (150 mg/kg), Saxenda (liraglutide, 0.1mg/kg), and combination of the two in an obesity model. We have found a disturbing difference in the tissue reaction of kidneys between the plant-based extract and the pharmacological agent with the combination group providing potentially valuable nephroprotective information. The Hoodia gordonii extract administered to the animals at a 30 and 45 days did not cause any histopathological deviation of the renal tissues. The fact that glomerular and tubular structures are not affected, and these findings can be seen in the light microscopy, means that there is no nephrotoxicity, even at the highest dose used (150 mg/kg). This is in line with previous reports that Hoodia is safe in traditional medicine use[15], and this hypothesis supports the hypothesis that bioactive phytochemicals of Hoodia have renoprotective effects.[16]

The lack of tubular necrosis, interstitial fibrosis, and glomerular enlargement in the Hoodia-treated sample proves the activity of plant-derived antioxidant in preserving renal tissue integrity. The pregnane glycosides and other bioactive compounds of Hoodia can have stabilizing properties on cell membranes and mitochondrial activity, which might be through free radical scavenging or through manipulation of inflammatory cascades.[17]

In contrast, sample treated with Saxenda (0.1 mg/kg) displayed clear signs of renal damage, consistent with early-stage drug-induced nephropathy. Histological abnormalities included glomerular hypertrophy, evidence of tubular epithelial cell necrosis, and interstitial infiltration by inflammatory cells. These observations echo findings in prior studies on glucagon-like peptide-1 (GLP-1) receptor agonists, where nephrotoxic manifestations have been linked to oxidative stress, impaired renal hemodynamics, and off-target metabolic effects.[18,19]

The low dose of this study (0.1 mg/kg) was chosen to represent the lower part of the therapeutic window in preclinical research, but even this relatively lower level of exposure caused tissue-level renal damage. This highlights the need to carry out additional safety assessment of chronic use of GLP-1 receptor agonists in groups with preexisting renal susceptibility.

Interestingly, the co-treated group (with Hoodia extract 150 mg/kg) before and during the administration of Saxenda portrayed an almost normal renal histology. The glomerular and tubular injury mitigation effect in this group indicates that the natural extract and the synthetic drug have a nephroprotective interaction.

The mechanisms by which this protective effect might be explained are likely to be several synergistic mechanisms:

1. Increasing of antioxidants defense: Hoodia extract can increase endogenous antioxidant enzyme activities, including superoxide dismutases (SOD), catalase, and glutathione peroxidases, and eliminate reactive oxygen species (ROS) generated by Saxenda.
2. Anti-inflammatory modulation: Bioactive phytoconstituents in Hoodia especially pregnane glycosides can inhibit pro-inflammatory cytokines including TNF- alpha and IL-6, which are involved in glomerular and tubular inflammation.[20]
3. Mitochondrial Preservation: Hoodia contains natural compounds that might stabilize mitochondrial membranes, inhibit cytochrome c release, and block the apoptotic cascade of events in renal tubular epithelial cells, which is often mediated by pharmacological nephrotoxins.[21]
4. Vascular stabilization and hemodynamic stability: Hoodia has the potential to induce renal perfusion and capillary stability indirectly and counteract the effect of Saxenda on disruptions in renal blood flow caused by changes in nitric oxide or endothelin.

CONCLUSION

Hoodia gordonii appears a harmless natural adjunct in the management of obesity, and it displays a protective effect on the nephrotoxicity of the medication as well as stimulates further preclinical and clinical studies in integrating plant-based therapy with pharmacological treatment to minimize the negative impacts of organ in association with drugs.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Zeinab Hameed Abbas, Dalal Abdel-Hussein Kadhim AL-Essawi
Drafting or Revising Critically:	Zeinab Hameed Abbas, Dalal Abdel-Hussein Kadhim AL-Essawi
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Oppert JM. Obesity: A major health issue in Europe. Int J Obesity Relat Metabol Disord 2002; 26(Supplement 4), S2-4.

2. Vettori V, Milani RV, Lavie CJ. Obesity and its impact on cardiovascular disease. Curr Atherosclerosis Reports 2019; 21(9): 38.
3. Vettori V, Farinetti A, Beneventi E, Manfredini R. The multifactorial origins of obesity: New insights and perspectives. Int J Environ Res Public Health 2021; 18(14): 7262.
4. Pagano C, Marin O, Calcagno A, Marchesi F, Pilon C, Urbanet R, Federspil G. Hormonal dysregulation in obesity and the metabolic syndrome. Ann New York Acad Sci 2005; 1083(1), 223–42.
5. Moon YS, Koh GY. Adipose tissue as an endocrine organ: Implications for the pathogenesis of obesity. J Metabol Res 2020; 12(3): 135–43.
6. Bhutani S, vanDellen MR, Cooper JA. Longitudinal weight gain and related risk behaviors during the COVID-19 pandemic in adults in the United States. Nutrients 2021; 13(2): 671.
7. Sarma S, Sockalingam S, Dash S. Obesity pharmacotherapy: A review of current and emerging treatments. Diabetes & Metabolic Syndrome: Clin Res Rev 2021; 15(6): 102280.
8. Lynn RM, Agrawal S. Anti-obesity pharmacotherapy: Current status and future perspectives. Therapeutic Advances in Endocrinology and Metabolism 2021; 12: 1–12.
9. Palm-Meinders IH, de Boer RA, van der Meer P. Safety and efficacy of GLP-1 receptor agonists: Emerging evidence from renal and pancreatic perspectives. Curr Diabetes Reports 2024;24(1): 15–27.
10. Alorfi NM, Alshehri MA. Liraglutide-associated renal and pancreatic adverse effects: a pharmacovigilance analysis. Saudi Pharmaceutical J 2023;31(1): 45–52.
11. Shukla Y, Kalra N, Taneja P. Anticancer potential of Hoodia gordonii: A brief review. Asian Pacific J Cancer Prevent 2009;10(4): 843–6.
12. van Heerden FR. Hoodia gordonii: a natural appetite suppressant. J Ethnopharmacol 2008; 119(3): 434-7.
13. Singh D, Singh RK, Chaturvedi VK. Herbal approach for obesity management: A review. International Journal of Pharmacy and Pharmaceutical Sciences, 2023; 5(2): 40-45.
14. Smith SA, Krygsman PH. Histopathological techniques in toxicological evaluation of anti-obesity agents. Toxicol Pathol 2014; 42(4):635-47.
15. van Heerden FR, van Wyk BE, Viljoen AM, Hamann T. Bitter principles of Hoodia gordonii: Isolation and structure elucidation of new steroid glycosides. J Ethnopharmacol 2008;119(3):558-63.
16. Shrivastava S, Patel TN. Phytochemical constituents and pharmacological activities of Hoodia gordonii: a review. J Pharmacognosy Phytochemistry 2020; 9(1): 145-50.
17. El-Hadary AE, Ramadan MF. Nutritional and therapeutic characteristics of Hoodia gordonii extract: Potential dietary supplement against obesity. Lipids Health Dis 2020; 19(1): 121.
18. Tuttle KR, Lakshmanan MC, Rayner B, Bonner C, Busch RS, Zimmermann AG, Brodows RG. Dulaglutide versus insulin glargine in patients with type 2 diabetes and moderate or severe chronic kidney disease (AWARD-7): A multicentre, open-label, randomised trial. The Lancet Diabetes & Endocrinology 2018; 6(8): 605-17.
19. Gilbert RE, Mende C. The role of GLP-1 receptor agonists in managing type 2 diabetes with renal impairment: focus on liraglutide. Clin Therapeutics 2019; 41(10): 1916-30.
20. Al-Sayed E, Esmat A, Khalil M, Hazem R. Anti-inflammatory and anti-arthritic activities of different fractions from Pluchea dioscoridis extract. BMC Complementary Alternative Med 2016; 16(1): 1-11.
21. Zhao L, Zou Y, Liu F, Zhou L, Chen Y, Hu C. Mitochondrial protection and anti-apoptotic effects of plant-derived compounds in renal ischemia-reperfusion injury. Phytomedicine 2019;58: 152871.