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Review Article

Histological Effects of Xenical and Efficiency Extract of Cinnamon on Renal Functions in Obese Male Rabbits

Marwa Adil Hameed[1*]

[1]Department of Anatomy and Histology, College of Veterinary Medicine, Tikrit University, Tikrit, Iraq

***Corresponding Author:** Marwa Adil Hameed
Department of Anatomy and Histology, College of Veterinary Medicine, Tikrit University, Tikrit, Iraq

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Abstract: This study investigated the detrimental effects of Xenical, both independently and in conjunction with cinnamon, on the histological alterations in renal tissue of obese male rabbits. The study evaluated the preventive properties of cinnamon extract by analyzing its ameliorative impact on the pathological alterations in renal tissue induced by the drug Xenical. Twenty mature male rabbits were categorized into two groups. Rabbits were administered chloroform anesthetic to induce unconsciousness, after which they were euthanized and dissected to obtain kidneys for pathological examination. Histological analysis of the kidney portion from the control group revealed the usual histological architecture of the renal cortex, characterized by prominent glomeruli and orderly renal tubules. The histological examination of kidney sections from the high-fat diet group was stained with hematoxylin and eosin, revealing an abnormal renal cortex, significant infiltration of inflammatory cells into the interstitial space, considerable glomerular atrophy, tubular necrosis, and marked alterations in the glomeruli, characterized by interstitial inflammation surrounding the glomeruli. Histological analysis of kidney sections from the high-fat diet and Xenical group, stained with hematoxylin and eosin, revealed mild histological improvements in cortical tissue, glomerular atrophy, dilation of Bowman's capsule, infiltration of interstitial inflammatory cells, and significant degeneration of tubular epithelium. Histological examination of kidney sections from the high-fat diet and cinnamon group, stained with hematoxylin and eosin, revealed significant histological improvements in renal cortical tissue, including normal glomeruli, normal tubules, slight infiltration of interstitial inflammatory cells, and mild degeneration. Histological examination of kidney sections from the high-fat diet and Cinnamon with Xenical group, stained with hematoxylin and eosin, revealed several histological alterations in renal tissue, including normal glomeruli with minor atrophy, normal tubules, slight infiltration of interstitial inflammatory cells, and pronounced congestion accompanied by mild degeneration and congestion.

Keywords: Xenical, Cinnamon, Renal functions, Male Rabbits.

INTRODUCTION

In 1997, the World Health Organization (WHO) classified obesity as a global epidemic threat based on an examination of body mass index (BMI) data. Since then, the incidence of obesity has markedly escalated and is now a critical public health issue. Obesity contributes to the onset of chronic diseases, including stroke, osteoarthritis, sleep apnoea, cancers, and inflammation-related disorders, as well as metabolic conditions such as diabetes, hypertension, and cardiovascular diseases (Elmaleh *et al*., 2023). Obesity, as a main illness, is defined by a positive energy balance. Identifying the fundamental causes of this imbalance, which account for the majority of cases detected after excluding secondary obesity-related factors, remains challenging. Intricate interactions among behavioural, genetic and environmental factors connected with lifestyle choices and socioeconomic position contribute to this chronic illness. Populations that endure a prolonged energy positive imbalance due to a sedentary lifestyle, a diminished resting metabolic rate, or both are more predisposed to obesity (Zou & Pitchumoni, 2023). Genes, metabolism, nutrition, physical activity, and the sociocultural environment are all contributing elements to obesity, which characterises the lifestyle of the twenty-first century. Identifying credible molecular targets that may be modified by external factors, like diet and pharmaceuticals, may assist individuals in managing their appetite and preventing obesity. Nutritional genomics may discover specific

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nutrients that induce phenotypic changes influencing obesity risk and ascertain the most critical interactions (Ghosh *et al*., 2023). It has been demonstrated to effectively mitigate the effects of obesity, including metabolic syndrome and endothelial dysfunction in all living individuals (Abdel-Baky and Abdel-Rahman, 2021). Xenical irreversibly inactivates lipases by covalently binding to the serine residues at their active sites. Consequently, triglycerides remain unhydrolyzed, preventing the absorption of free fatty acids. Xenical predominantly exerts its effect by inducing a localised lipase obstruction in the stomach (Jin *et al.*, 2021). Xenical operates without systemic absorption, decreasing dietary fat absorption by around 30% (Braeckmans *et al*., 2022). Despite Xenical selective action, numerous studies have identified significant adverse effects. The most common gastrointestinal side effects include dyspepsia, diarrhoea, flatulence, and abdominal pain (Adeyemi *et al*., 2020). It directly damages intestinal villi during metabolism in the gastrointestinal tract. Additionally, malabsorption leads to deficiencies in fat-soluble vitamins (ADEK). Research indicates that Xenical inhibits carboxylesterase-2, a crucial detoxification enzyme, thereby heightening the risk of severe liver, pancreatic, and renal damage. The oral cavity is also affected by various anomalies resulting from the side effects of this anti-obesity medication (Uehira *et al*., 2023). Cinnamon, a herbaceous plant, belongs to the Lauraceae family. Cinnamon is one of the most extensively utilised spices globally, employed both as a flavouring agent in culinary applications and in medical formulations, owing to its physiological properties. For ages, diverse cultures globally have employed cinnamon as a culinary flavouring agent owing to its organoleptic characteristics (Abeysinghe *et al*., 2020). This study research conducted to:

1. Investigate the Histological side associated with the use of Xenical alone and when combined with cinnamon at the level of renal tissue changes in obese Male Rabbits.
2. Assessment the Protective effects and activity of antioxidant Properties of extract cinnamon, by its improved effect on the pathological changes induced by the drug Xenical in kidney tissue.

Preparation of Xenical

Drug: (Xenical ®, Jordan). A commercially accessible formulation of 120 mg per capsule was acquired from a local private pharmacy. It was reconstituted in normal saline and supplied at a dosage of 10 mg/kg of body weight.

Preparation of Cinnamon Extract

Preparation of cinnamon involves adding 100 grams to 2000 milliliters of water. After boiling for two minutes, the infusion is allowed to cool to room temperature before being filtered (Yulianto *et al*., 2021).

Animals Experimental

In this investigation, twenty male rabbits with weights ranging from 1400 to 1800 grams were utilized. Obtained from the College of Veterinary Medicine, Tikrit University – Iraq, the animals, aged between 12 to 15 weeks, were housed in suitable conditions within specialized plastic cages. They are afforded suitable conditions and ventilation. The lighting system operated for 12 hours daily, with a relative humidity of 50 ± 5%. They were maintained for two weeks to acclimate to conventional experimental conditions. The experiment commences on October 1st and concludes on December 30th. The temperature was regulated the room air was continually exchanged at a temperature range of 21-25°C using a room thermostat. Administer a pellet of fresh food ration to the animals utilizing vacuum ventilation.

Experimental Design

The animals were divided into five groups

1. Control group: 4 rabbits received only a normal diet without fat as a daily dose for six weeks.
2. High fat diet group: 4 rabbits received only fed with high-fat diet contain (Plate with soy fat) and introduce as daily for six weeks (Oliveira., 2020).
3. Group high fat diet with Xenical 4 rabbits (10 mg/kg/day) (Zakaria *et al*., 2021).
4. Group high fat diet with cinnamon 4 rabbits (100 mg/kg BW) (Li *et al*., 2022).
5. Group high fat diet with Xenical (10 mg/kg/day) and cinnamon (100 mg/kg BW) 4 rabbits.

Histological Study

After the experimental length, all animals were subjected to deep chloroform anesthesia, euthanized, and the organ of interest was excised. Subsequent to a brief rinsing with tap water, they were promptly submerged in a 10% formal saline solution. The sections were stained using standard hematoxylin and eosin (H&E) procedures. Microscopy images of each section were acquired using a light microscope and a Canon digital imaging apparatus from Japan for analysis.

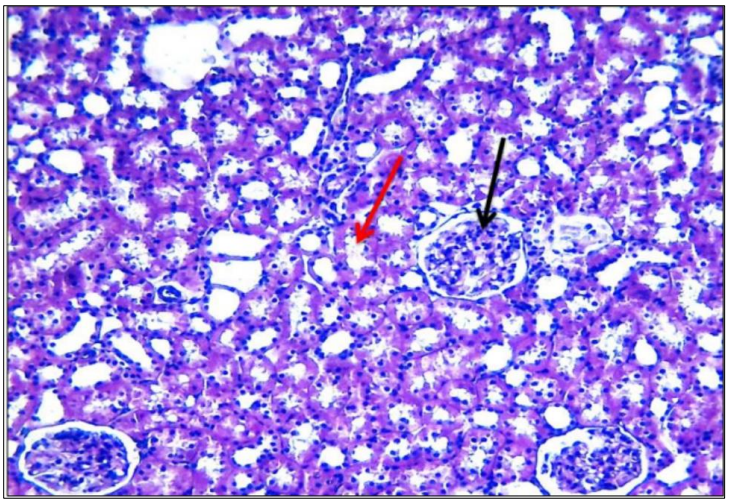

Figure 1: Photomicrograph of rabbit kidney tissue from the control group, exhibiting the normal histological architecture of the renal cortex with prominent glomeruli (black arrow) and orderly renal tubules (red arrow). (Hematoxylin and Eosin, 10X)

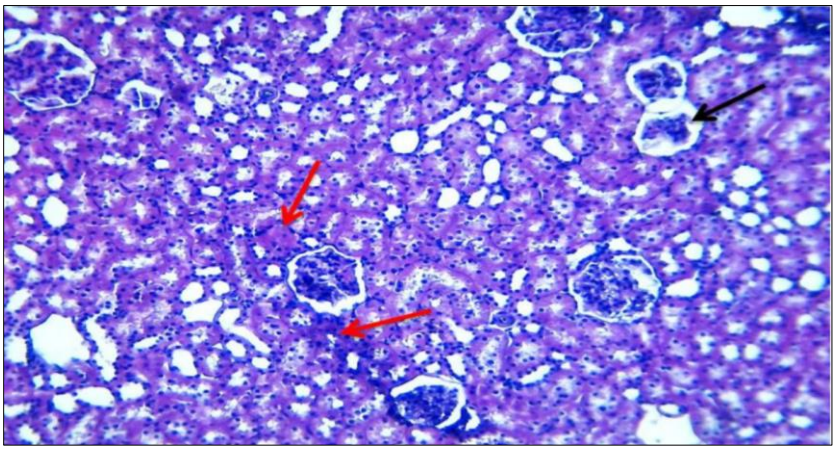

Figure 2: Photomicrograph of rabbit kidney tissue section from a high-fat diet group, illustrating the aberrant morphology of the renal cortex, pronounced glomerular atrophy (black arrow), and regions of tubular necrosis (red arrow).(Hematoxylin and Eosin, 10X)

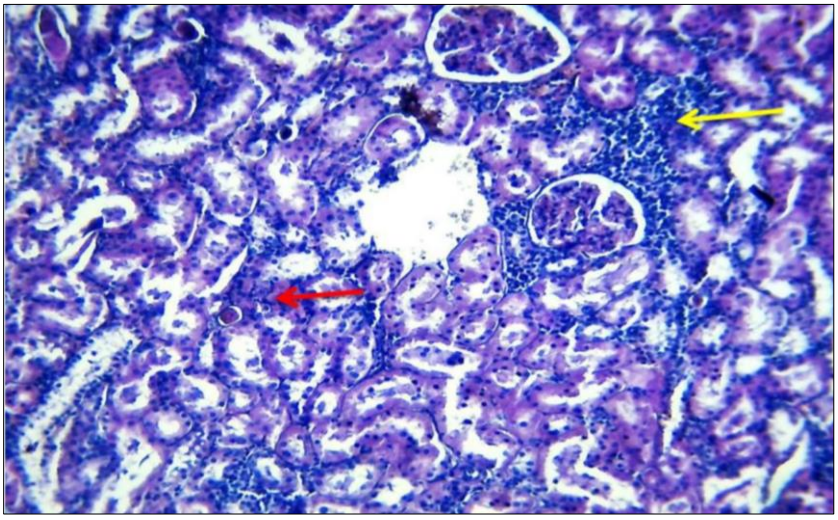

Figure 3: Photomicrograph of rabbit kidney tissue section from a high-fat diet group, illustrating the aberrant morphological characteristics of the renal cortex, significant interstitial infiltration of inflammatory cells (yellow arrow), and regions of tubular necrosis (red arrow).(Hematoxylin and Eosin, 10X)

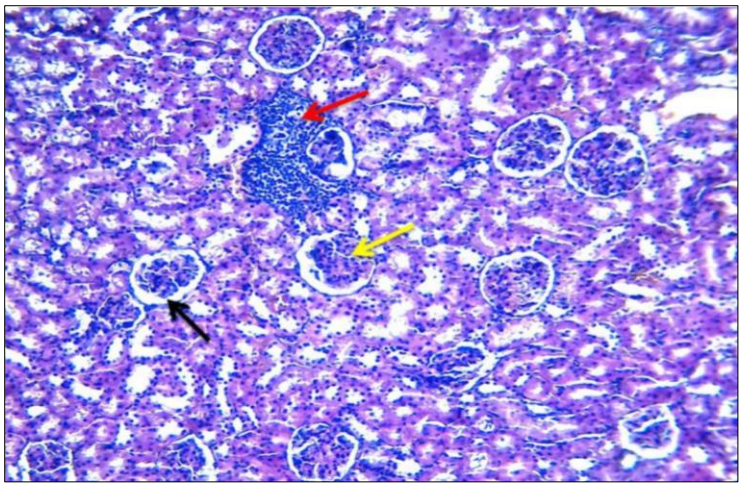

Figure 4: Photomicrograph of rabbit kidney tissue section from a high-fat diet and Xenical group, demonstrating mild histological improvements in cortical tissue, glomerular atrophy (yellow arrow), dilation of Bowman's capsule (black arrow), and infiltration of interstitial inflammatory cells (red arrow).(Hematoxylin and Eosin, 10X)

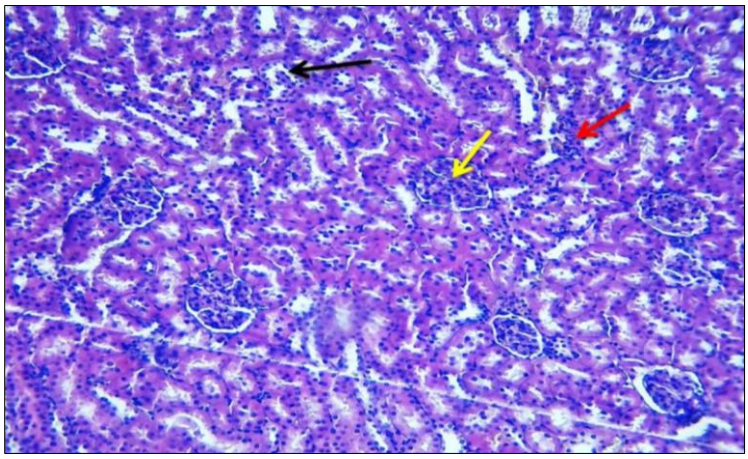

Figure 5: Photomicrograph of rabbit kidney tissue section from a high-fat diet and cinnamon group, demonstrating significant histological enhancements in renal cortical tissue, normal glomeruli (yellow arrow), normal tubules (black arrow), and slight infiltration of interstitial inflammatory cells (red arrow).(Hematoxylin and Eosin, 10X)

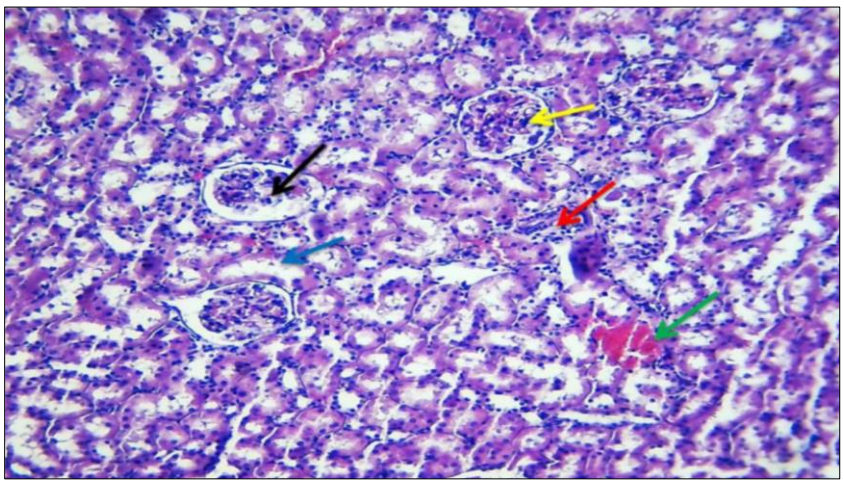

Figure 6: Photomicrograph of rabbit kidney tissue section from a high-fat diet and Cinnamon with Xenical group, illustrating various histological alterations in renal tissue, including normal glomeruli (yellow arrow) with minor atrophy (black arrow), normal tubules (blue arrow), slight infiltration of interstitial inflammatory cells (red arrow), and pronounced congestion (green arrow).(Hematoxylin and Eosin, 10X)

After the animals underwent anesthesia, the kidney was excised, and subsequent to fixation, sections of the kidney were procured and preserved in formalin (10%). After processing in alcohol and paraffin, the samples were sectioned and subsequently stained with hematoxylin and eosin (H&E). Histological examination of kidney sections from the control group was conducted using hematoxylin and eosin staining, revealing the normal histological architecture of the renal cortex, characterized by prominent glomeruli (black arrow) and regular renal tubules (red arrow), as illustrated in Figure 1. (Demiraslan *et al*., 2024). Histological analysis of kidney sections from the high-fat diet group was conducted using hematoxylin and eosin staining, revealing abnormal characteristics of the renal cortex, pronounced infiltration of inflammatory cells into the interstitial space, significant glomerular atrophy and tubular necrosis, as well as marked alterations in the glomeruli, evidenced by atrophy and interstitial per glomerular inflammation, as illustrated in figures (2) and (3). (Ramadan *et al*., 2016). A high-fat diet is characterized by perivascular and per glomerular edema infiltrated with many inflammatory cells, accompanied by dilated blood vessels (Othman *et al*., 2022). Evidence of glomerular capillary and major blood vessel dilation was present. Comparable results were observed for histologically identified glomerular atrophy, necrosis, and edema, along with tubular deformations. The renal enlargement noted in HFD-fed rabbits may be ascribed to edema caused by the infiltration of mononuclear cells within the tubules, suggesting that dilatation could lead to an increase in kidney volume (Yang *et al*., 2024). Histological analysis of kidney sections from the high-fat diet and Xenical group, stained with hematoxylin and eosin, revealed mild histological improvements in cortical tissue, glomerular atrophy, dilation of Bowman's capsule, infiltration of interstitial inflammatory cells, and significant degeneration of tubular epithelium, as illustrated in Figure 4 (Jin *et al*., 2023). The administration of Xenical to HFD rabbits induces several histological changes in kidney tissue, as evidenced by the light microscopy findings undertaken to far (Eleazu *et al.,* 2022). The alterations consist of: (a) a hypermetric glomerular tuft associated with hypertrophy of the renal tubule lining epithelium and (b) a vacuolar glomerular tuft including larger endothelial cells lining the Bowman's capsule (Sabik *et al*., 2022). The administration of Xenical resulted in degeneration of specific renal tubules, accompanied by a focal necrotic region characterized by inflammatory cell infiltration and engorged blood vessels (Bays *et al*., 2022). High-fat diets elevate serum uric acid levels, leading to renal urate crystal formation and subsequent histological changes. Urinary oxalate levels were significantly increased by Xenical, especially in rabbits fed high-fat or oxalate-enriched diets (Al Obaidi & Rzoqi, 2023). Our histological examination of renal tissue revealed that Xenical induces renal damage by distending Bowman's capsule and resulting in glomerular atrophy and disruption of specific renal tubules. It is posited that hyperoxaluria is the underlying cause of these pathological renal effects linked to Xenical, occurring when fats are inadequately absorbed in the small intestine, leading to health complications (Al-safo & AlDulaimi, 2022). Moreover, the impact of Xenical on renal function indicated that the medication may elevate the risk of acute renal injury, nephrolithiasis, and oxidative nephropathy, characterized by a localized necrotic region with inflammatory cell infiltration due to Xenical administration (Verma *et al*., 2023). Histological analysis of kidney sections from the high-fat diet and cinnamon group, stained with hematoxylin and eosin, demonstrated significant histological improvements in renal cortical tissue, including normal glomeruli, normal tubules, slight infiltration of interstitial inflammatory cells, and mild degeneration, as illustrated in figures (5) (Sobhey *et al*., 2023). Impact of prolonged high-fat diet on renal levels and cinnamon's capacity to mitigate HFD toxicity. Cinnamon has significant amounts of potent antioxidants known as flavonoids and phenolic components. Numerous research have investigated cinnamon's antioxidant efficacy against various agents' HFD (Tekeli *et al*., 2021). In this study, rabbits administered cinnamon alongside a high-fat diet consistently exhibited significant the findings indicate a significant enhancement in renal function. Cinnamon may exert a protective influence on the kidneys against oxidative damage induced by a high-fat diet by augmenting antioxidant defense system activity, neutralizing reactive oxygen species, and inhibiting lipid peroxidation. This is attributed to cinnamon's elevated levels of flavonoids and phenolic compounds, which serve as powerful antioxidants (Aslam *et al*., 2023). Histological examination of the kidney revealed normal glomeruli and tubules. Additionally, normal kidney shape was noted, since it was reported that cinnamon safeguards the kidney by mitigating glomerular enlargement and diminishing tubular dilations (Idoko *et al*., 2023). Histological analysis indicated that the convoluted tubule next to the kidney exhibited the most severe damage; however, this damage was markedly mitigated with cinnamon administration, resulting in the preservation of these components in the urine (Ghonim *et al*., 2017). Histological analysis of kidney sections from the high-fat diet and Cinnamon with Xenical group, stained with hematoxylin and eosin, revealed several histological alterations in renal tissue, including normal glomeruli with minor atrophy, normal tubules, slight infiltration of interstitial inflammatory cells, and pronounced congestion accompanied by mild degeneration, as illustrated in figures (6) (Hamden, 2022). Pathological structural abnormalities in the kidneys of rabbits were examined in a group fed a high-fat diet in conjunction with rabbits administered cinnamon and Xenical. Our analyses indicated that the combination therapy markedly modified the kidney's structural attributes, characterized by the eradication of substantial cellular damage and necrosis, the lack of inflammatory cell infiltration, and the absence of tubular dilation with uniform cellular morphology (Alshahrani *et al*., 2021). However, a combination of Xenical and cinnamon mitigated cellular damage in rabbits subjected to a high-fat diet. Moreover, the histological analysis corroborated that the combination of cinnamon and Xenical, administered alongside a high-fat diet, resulted in non-cellular alterations, including ameliorated tubular damage and less renal necrosis. However, the new study indicates that a high-fat diet combined with cinnamon and Xenical enhances cellular morphology due to their strong antioxidant properties, which also aid in fortifying and mitigating renal damage (Hussain *et al*., 2023).

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