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Histological changes in the brain and liver of high-fat diet-fed male rats as a result of orlistat administration

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ABSTRACT

Obesity is a disorder characterized by excessive body weight gain. Orlistat is one of the medications used in the treatment of obesity, and acts by inhibiting gastric and pancreatic lipases. The objective of this study was to examine the short-term effects of orlistat on liver and brain tissues in rats fed a high-fat diet. In this study, 20 male albino rats (weighing approximately 193–212 g) were divided into two groups: group I (control group; consisting of five rats administered distilled water daily) and group II (orlistat group; comprising 15 rats given a daily oral dose of orlistat at a dose of 32 mg/kg body weight per day, *via* gastric tube, for 10 weeks). At the end of the experimental period, the animals were sacrificed, and the liver and brain tissues were prepared for histological analysis. Rats treated with orlistat exhibited degenerative changes in both liver and brain tissues compared to the control group. In the liver, these changes included dilation, blood vessel congestion, and lymphocyte infiltration. In the brain, the observed changes were characterized by the infiltration of neutrophils or mononuclear leukocytes. In conclusion, orlistat exerts harmful effects on liver and brain tissues; therefore, its clinical use should be closely monitored.

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1. Introduction

Obesity is one of the leading causes of mortality worldwide. It is considered by health professionals to be one of the most significant public health challenges of the twenty-first century[1]. In order to address weight-related disorders, a lipophilic medication known as

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orlistat (Xenical) is commonly used. Orlistat is a gastrointestinal lipase inhibitor that treats obesity by preventing the absorption of dietary fat. By inhibiting pancreatic lipase, it allows approximately 30% of dietary lipids to pass through the intestine undigested[2]. It is available in 120-mg capsule form. Xenical is prescribed for individuals with a body mass index (BMI) of 30 or higher, or for overweight individuals (BMI≥28) who are at risk of obesity-related diseases. It should not be used if a meal is skipped or contains no fat[3]. Severe adverse effects of Xenical include intense abdominal pain, haematuria, shortness of breath, loss of appetite, and jaundice. It should not be used by individuals allergic to its components[4]. The aim of this study was to examine the short-term effects of orlistat on liver and brain tissues in rats fed a high-fat diet.

2. Methodology

Twenty male albino rats (weighing approximately 193–212 g) were used in this study, conducted between December 2022 and March 2023 at the Animal House of the College of Pharmacy of the University of Babylon. The animals were fed a high-fat diet obtained from Research Diets (New Brunswick, USA), were given tap water, and were maintained under controlled environmental conditions. All procedures adhered to the guidelines of the institutional ethics committee (approval date: 11/03/2022; protocol no.: A-0014). After a 1-week acclimation period, the rats were divided into two groups: group I (consisting of five healthy control rats that received distilled water daily) and group II (comprising fifteen rats administered orlistat dissolved in distilled water, *via* gastric tube, at a dose of 32 mg/kg body weight per day, for 10 weeks). Orlistat was supplied by the Hikma Pharmaceutical Company (Jordan). At the end of the experimental period, the animals were sacrificed. Liver and brain tissue samples were collected from each rat and were prepared for histological analysis following the methodology described by Suvarna *et al.*[5]. Tissue sections were examined and photographed using a light microscope.

3. Results

As shown in Figures 1A–1C, the liver tissue of control rats appeared normal, whereas orlistat-treated rats exhibited pathological changes such as dilation, vascular congestion, and lymphocyte infiltration. Similarly, while the brain tissue of control rats maintained normal architecture (Figure 1D), the brain tissue of orlistat-treated rats showed signs of inflammation (Figure 1E).

4. Discussion

In the present study, orlistat administration induced histological alterations in the liver and brain tissues of male rats that were fed a high-fat diet. The lymphocyte infiltration observed in the liver tissues is consistent with previous findings[6,7], suggesting that reactive oxygen species and lipid peroxidation products may cause mitochondrial dysfunction leading to apoptosis and necrosis, and initiating a cascade that results in fibrosis and collagen deposition. Filippatos *et al.*[8] have also reported mononuclear cell infiltration associated with the release of inflammatory mediators (such as tumour necrosis factor-alpha), which are likely contributors to liver damage. In our study, the orlistat-treated group exhibited significantly dilated and congested hepatic vessels, aligning with previous reports of congested portal and central veins[7]. The observed vascular dilation may reflect metabolic disturbances in the liver, thereby suggesting a potential hepatotoxic effect of orlistat[7].

Histological abnormalities in brain tissue were noted in group II, including infiltration by neutrophils and mononuclear leukocytes. Immune cell-mediated inflammation is a key mechanism linking obesity to insulin resistance, and may underlie the observed brain damage[9]. Additionally, orlistat has been shown to alter the histological structure of the hypothalamus, thereby affecting levels of various neuropeptides and central monoamine neurotransmitters[9].

5. Conclusion

Our study concludes that orlistat can induce patho-

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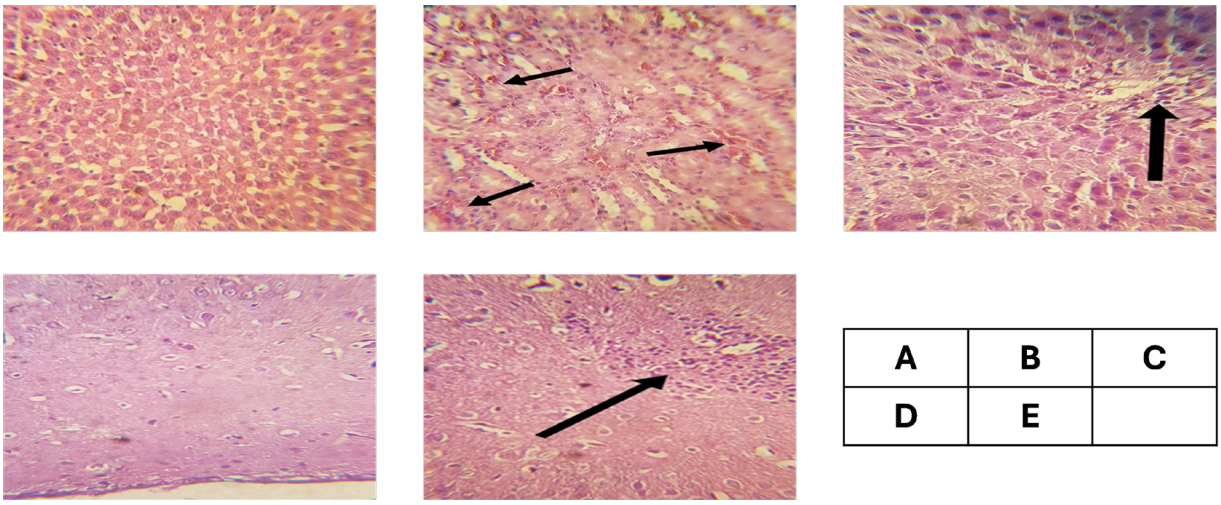

Figure 1. *Microphotographs of rat liver and brain tissue sections, stained with haematoxylin and eosin (×400). (A): Liver tissue section from a group I (control) rat showing normal histological architecture. (B): Liver tissue section from a group II (orlistat-treated) rat displaying dilated and congested blood vessels (black arrows). (C): Liver tissue section from a group II (orlistat-treated) rat showing lymphocyte infiltration (black arrow). (D): Brain tissue section from a group I (control) rat exhibiting normal histological structure. (E): Brain tissue section from a group II (orlistat-treated) rat showing infiltration by neutrophils or mononuclear leukocytes (black arrow).*

logical changes in liver and brain tissues. Therefore, its use should be closely monitored by healthcare professionals, and patients should be observed for any unusual symptoms.

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Conflicts of interest

None exist.

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