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Ministry of Higher Education

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University of Babylon

College of pharmacy

Histological study of the effect of orlistat on stomach, small intestine and pancreas of adult albino rats

A Research Project

Submitted of the Council College of pharmacy, University of Babylon in practical Fulfillment of The Requirement for The Degree of Bachelor's in pharmaceutical sciences

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بِسْمِ اللَّهِ الرَّحْمَـٰنِ الرَّحِيم

" وَقُلْ رَبِّ زِدْنِي عِلْمًا "

صدق الله العلي العظيم

سورة طه الآية (114)

Dedication

Dedicated to,

Our parents who taught us to believe in ourselves

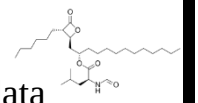
our teachers who used to lead us to light,

to army men who spread peace,and finally, to our supervisor who helped us along the project work time,

INTRODUCTION

Orlistat, sold under the brand name Xenical among others, is a medication used to treat obesity. Its primary function is preventing the absorption of fats from the human diet by acting as a lipase inhibitor, thereby reducing caloric intake. It is intended for use in conjunction with a healthcare provider-supervised reduced-calorie diet.[1]

Orlistat is the saturated derivative of lipstatin, a potent natural inhibitor of pancreatic lipases isolated from the bacterium *Streptomyces toxytricini*.[2] However, due to its relative simplicity and stability, orlistat was chosen over lipstatin for development as an anti-obesity drug.[3]



The effectiveness of orlistat in promoting weight loss is definite but modest. Pooled data from clinical trials suggest that people given orlistat in addition to lifestyle modifications, such as diet and exercise, lose about 2–3 kilograms (4–7 lb) more than those not taking the drug over the course of a year.[4] Orlistat also modestly reduces blood pressure and appears to prevent the onset of type 2 diabetes, whether from the weight loss itself or other effects. It reduces the incidence of diabetes type II in people who are obese around the same amount that lifestyle changes do.[5]

Benefits aside, however, orlistat is noted for its gastrointestinal side effects (sometimes referred to as *treatment effects*), which can include steatorrhea (oily, loose stools). They decrease with time, however, and are the most frequently reported adverse effects of the drug.[6]

AIM OF STUDY

Is to determine the histological changes in GIT tissue after chronic administration of orlistat.

MATERIAL AND METHODS: -

In this investigation, ten rats (about 193-212 mg), during the period from December 2022 to March 2023. It has been achieved in the Animal House of Faculty of Pharmacy Babylon University. All animal experiments comply with the guidelines and should be carried out in accordance with the U.K. Animals.

The animals were maintained under controlled environmental conditions and were provided with a free access to high protein diet and tap water. After one week acclimatization period, the animals were randomly divided into two groups as follows: Group 1 (G1): 5 Healthy control rats. Group 2 (G2): 5 Rats of this group were received orlistat dissolved in DW orally by a gastric tube at a dose of 0.8 mg/kg /day [(7)].

Histological study According to Bancroft's idea, histological sections of the small intestine, stomach and pancreas (5 thick) were generated to evaluate the alterations that may be discovered in the treatment animal groups compared to the control group. [8]

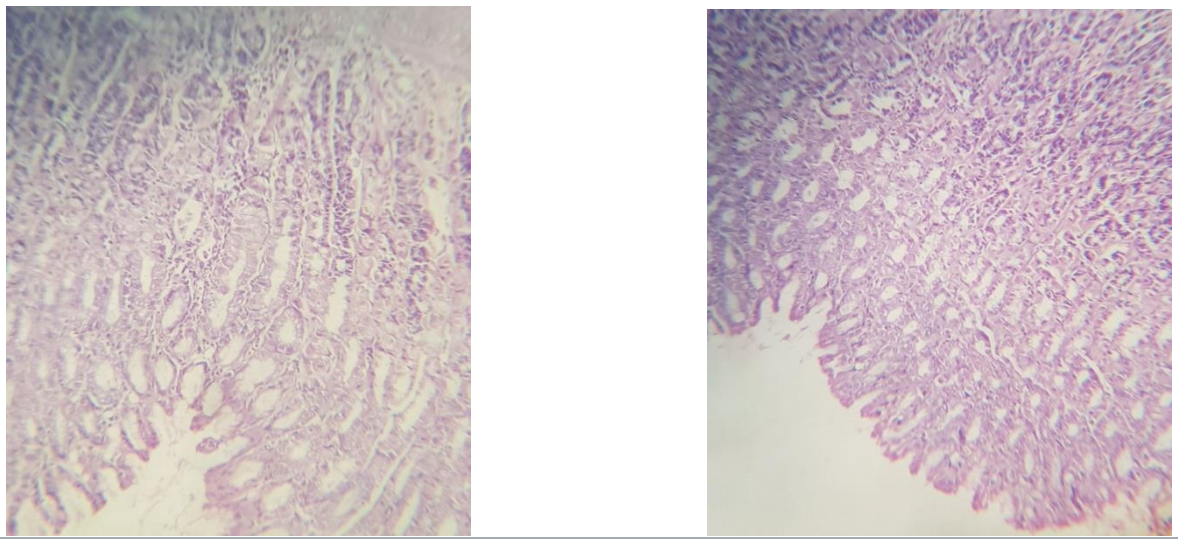
Chemical and medicine

Orlistat capsule was used in this experiment 'Xenical', it was dissolve in warm DW and administered to each rat in oral tube (5 ml of DW for dissolving 1.4 mg of orlistat). Treatment was done once daily for a continuous 70 days.

The Result

In (figure 1) the control group (group I) showed normal histological structures of stomach , while the orlistat treated group (group II) showed normal histological structures of stomach

In (figure 2) the control group (group I) showed normal histological structures of small intestine tissue, while the orlistat treated group (group II) showed normal histological structures of small intestine tissue Also, in (figure 3) control group (group I) showed normal histological structures of pancreas tissue , while the orlistat treated group (group II) showed dilated, congested blood vessels of pancreas.

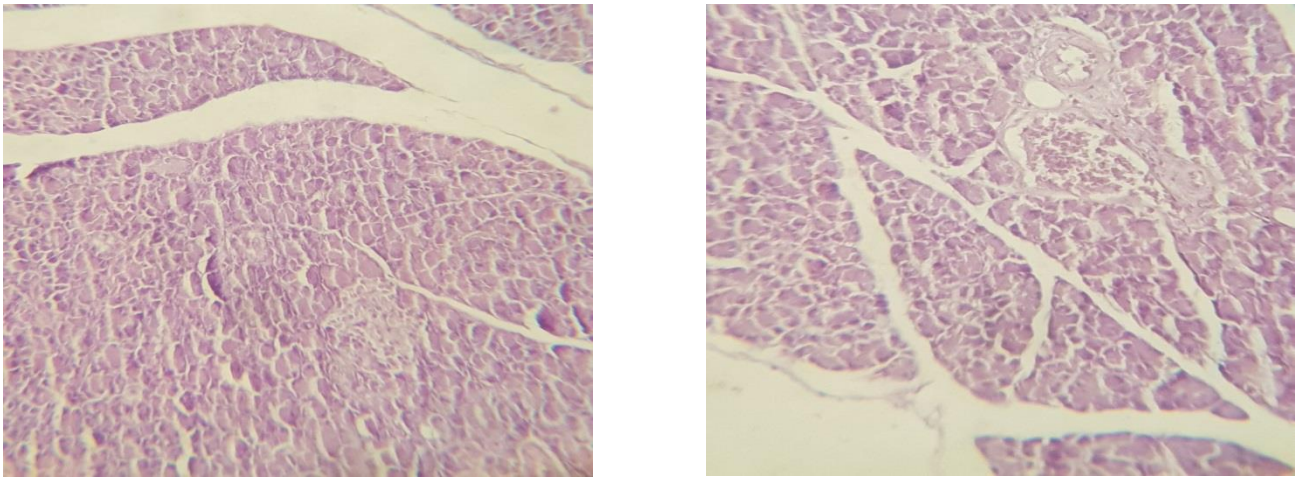


(A) (B)

Figure (1) Cross section of stomach: A group I the control group showing normal architecture of stomach tissue (B) Group II the treated group with orlistat showing normal histological structures of stomach tissue.

(A) (B)

figure (2) Cross section of small intestine: A group I the control group showing normal architecture of small intestine tissue (B) Group II the treated group with orlistat showing normal structures of small intestine tissue.



(A) (B)

figure (3) Cross section of pancreas: A group I the control group showing normal architecture of pancreas tissue (B) Group II the treated group with orlistat showing dilated, congested blood vessels.

Discussion

Obesity is a significant health problem that is growing in prevalence [9]. Orlistat (Xenical; Roche, Basel, Switzerland), has been introduced at the end of 1998 and represented as a magic medicine for obesity without pain of dieting. The drug is licensed for patients with BMI >28 kg/m2 but many adverse effects were observed such as pancreatitis [10]. an inhibitor of pancreatic lipases that limits the intestinal absorption of dietary fat, has proven effective in augmenting weight loss [11]. Currently, orlistat is the only FDA (Food and Drug Administration) approved drug for long term management of obesity [12]. It has been reported that there has been an association between the use of orlistat and development of pancreatitis in some cases clinically with no evidence of biliary disease or alcohol consumption [13]. This study is concerned with the description of structural changes in pancreas, small intestinal and stomach in male rat following orlistat administration and whether these effects are dose dependent or not.

In our experiment, stomach and small intestine tissues showing normal histological structures may reflect the safe or harmless effect of Orlistat on these tissues , while the orlistat treated group (group II) showing dilated, congested blood vessels in pancreas tissue.

In accordance with these results, it has been reported by Elbakary *et al.* that there was an increase of interlobular connective tissue with dilated congested blood vessels (14).

Same studies revealed that orlistat induced histological and ultrastructural changes in the exocrine part of the pancreas. Dilation and congestion of the blood vessels, which were detected in this study, were explained by excess production of NO arising from inducible NO synthase, which may be an important factor in the systemic and local homodynamic disturbances(15)

Conclusion

It was suggested that orlistat can induce pancreatitis, and hence it must be used under medical observation. Thus, it is necessary to pay more attention to the side effects of orlistat on pancreatic function particularly in patients at risk of pancreatic injury.

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