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The Harmful Effect of a Slimming Drug Compared to a Mix of Some Plants Extract on Rats

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ABSTRACT

Background: Xenical drug impact was used for studying losing weight by testing some physiological parameters in male rats compared to (Hatra herbs®) plants extract used for slimming .

Methods: ALT,AST,ALP,B.UREA Creatinine, lipids profile, TSH, T4 and T3 were examined. male rats separated into 3 groups: control group, a Xenical group (120 mg\kg b.wt) and a mix plants extract group (200 mg\kg b.wt).

Result: Results showed that body weight, cholesterol, triglyceride, VLDLand LDL had a significant drop in plants extract group compared to control, whilst ALTandAST showed a substantial rise in Xenical group compared to control also a significant surge in ALP in both treated groups compared to control . on other hand had, T3 and TSH had a significant reduced in Xenical group, while T3 showed non significant differences in plants extract group compared to control ,in the meantime T4 exhibited increased significance in Xenical group and non significant differences in plants extract group compared to control. B.urea showed a significant escalation in Xenical group compared to plants extract group and control, while creatinine noted no significant differences in all treated groups compared to control group.

Key words: Creatinine, Lipids profile, Mice, TSH, UREA, Xenical.

INTRODUCTION

Obesity has been described as an excessive body fat accumulation so that may elevated risk in the individual health (Woolcott *et al.*, 2018) and it is rated that over one billion adult the world are overweight and at least one to third of this category from population are assorted as obese. A body mass index (BMI) more than 25 considered overweight and over 30 obese, therefor several factors participate to an individual's capability to get weight like genetic predisposition, age and environmental agents. Actually the main causes of obesity are decrease exercises as well as increase intake of high energy foods (Chong *et al.*, 2018; Drew *et al.*, 2007), thus for obesity treating clinical therapy must be started by changing life style and focus on behavioral alternation, physical activity and diet. Weight reduction drugs or anti-obesity medication are all pharmacological agent that control or decrease weight. These drugs alter one of essential processes of individual´s body, including alters intestinal absorptionorchanging appetite. Some prescriptions of weight loss medicine are stimulants, which are recommended to use for short-term only, therefore they of limited usefulness for very obese patients, who may need to reduce weight more than months.At the end of 1998 Roche pharmaceutical firm has introduced Orlistat(Xenical) in UK and has been approved in 1999 by Food and Drug Administration (FDA) for weight-loss (Pi-Sunyer *et al.*, 1996; Anees *et al.*, 2024), this medicine received great attention around the world and the company assumed that it had fewer side effects, but what has been discovered later was quite the opposite. It was a new pharmacological therapy reduce fat absorption by reversibly inhibiting gastric and pancreatic lipases, these lipases have an essential role in digestion fat by breaking down the triglycerides in to absorbable free fatty acids and monoglycerides. Orlistatparticipate binds to the active sites of lipases and inactivates them so the inactivation of lipases prevents the hydrolysis of triglycerides and thus free fatty acids are not absorbed (Nicholls *et al.*, 2001; Humayun *et al.*, 2016). Xenical was supposed to be dedicated for people with a body mass index (BMI) 28 kg/m^2 or 30 kg/m^2 in the existing of obesity-associated complication, the usage of Xenical has been related with many mild-to-moderate gastrointestinal adverse effects (Hsieh *et al.*, 2005). The essentially side effects of this medicine are

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digestion process-related, including steatorrhea (oily and soft fecal with too match flatus due to unabsorbed fats reaching toward the large intestine), incontinence and frequent gut movements and also gastrointestinal adverse state like, esophagitis and abdominal ache in few (Filippatos *et al.*, 2008). To reduce these effects the company advises people tofollow a low-fat diet or avoidhigh fat content foods to control the oily stool and flatulenceas well as minify calorie in their meals (Ghosh *et al.*, 2021). There are many studies showed that 8.8% of Xenical consumers stopped their treatment due to adverse events, furthermore many cases of severe liver damage had been registered (Lehmann *et al.*, 2011) and the suggested mechanism for liver damage is hypersensitivity because only small amount of Xenical is absorbed (Nwobodo *et al.*, 2015). At the same time several studied indicated that many of obese patients had a developed gallbladder abnormalities diagnosed by ultrasound, as well as renal abnormalities (cysts and stones) developed in other Xenical treated (Heck *et al.*, 2000; Kang *et al.*, 2012). On the other hand increase the risk of urea and creatinine elevation then an acute kidney damage, this occurs when the unabsorbed fat bind with calcium in the intestinal lumen resulting excessive oxalate, which eventually absorbed and deposited in kidney leading to oxalate nephropathy then increase renal stones formation (Cristina *et al.*, 2024).

MATERIALS AND METHODS

Animals

In this experiment, 18 albino rats were used, with an average weight of 175±10, at 5-6 weeks of age, were divided into three equal groups, which they control group, treated group with 120 mg\kg of Xenical® drug, treated group with 200 mg\kg of mix plants extract (Hatra herbs®) which involved Green tea, Pimpinella (anise), Foeniculum vulgare (fennel), Coriandrum sativum(Coriander) and Carum carvi (Caraway). Animals were treated orally by gavage tube for 60 days. All rats were received diet and water ad libitum.

Blood and serum samples

At the end of the trial, rats were deprived for the whole night. Rats from each group were killed with sodium pentobarbital and then thoroughly dissected. To extract and separate the serum from the inferior vena cava, centrifugation was performed for 15 minutes at 3000 rpm. In order to analyze and estimate blood parameters, the serum was kept at -18°C.

Hormone assay

Total testosterone levels were calculated in sera using the methodology of Alankooshi *et al.* (2023); Alyasiri *et al.* (2024) whilst serum TSH and T3 and T4 levels were determined using the methods of Odell *et al.* (1967, 1974).

Biochemical analysis

The method of Peterson *et al.* (1997) was used to estimate AST, ALT, ALP and B.urea, creatinine in sera, whereas the method of Hameed (2023); Hasan *et al.* (2024); Hasan *et al.* (2023); Hameed *et al.* (2024) was utilized to estimate liver function and kidney function in sera, respectively.

RESULTS AND DISCUSSION

The results showed a significant decreased in body weight of group treated with Xenical and group treated with mix plants extract at the first day of experiment compared with body weight at the end of experiment for both groups, while the results show a significant increase of body weight of control group at the end of experiment (Table 1).

Regarding lipid profile, there was a significant decrease in cholesterol level in the treated group Xenical and group treated with mix plants extract compared with control group. The results also showed a significant decrease in the level of Triglyceride in both treated group with Xenical and mix extract respectively compared with control group. The results also obtained a significant increase in the level of HDL in group treated with Xenical)and mix extract, while the results recorded a significant decrease in LDL in group treated with Xenical and mix extract compared with control group and significant decrease in VLDL in group treated with Xenical and mix extract compared with control group.On other hand the results revealed a significant decrease in glucose level in group treated with Xenical and mix extract compared with control group (Table 2).

Table 1: Comparison between the effect of Xenical drug and mix plants extract on body weight in rats.

Groups	Inetial body weight	Final body weight	LSD
Control	180.54±3.87^{a}	190.63±4.09^{b}	3.64
Xenical 120 mg\kg	185.53±3.90^{a}	165.53±3.87^{b}	4.73
Mix plant 200 mg\kg	182.78±2.43^{a}	173.96±1.84^{b}	3.90

Means having with the different letters in same row differed significantly. *(P≤0.05).

Table 2: Comparison between the effect of Xenical drug and mix plants extract on lipid profile in rats.

Groups	Cholesterol mg\dl	Triglyceride mg\dl	HDL mg\dl	LDL mg\dl	VLDL mdl	Glucose mg\dl
control	110.53±1.74^{A}	95.33±2.97^{A}	37.74±0.76^{c}	54.44±4.74^{a}	19.21±0.96^{a}	112.54±3.95^{a}
Xenical 120 mg\kg	85.52±1.74^{C}	80.12±5.23^{C}	40.31±1.66^{b}	29.03±.2.80^{c}	16.07±1.67^{b}	80.93±5.90^{b}
Mix plant 200 mg\kg	95.68±1.74^{B}	84.09±1.90^{B}	45.98±2.07^{a}	34.28±2.62^{b}	16.41±1.06^{b}	85.22±3.64^{b}
LSD	4.86	2.79	2.82	3.42	2.60	5.73

Means having with the different letters in same column differed significantly. *(P≤0.05).

Concerning thyroid hormones, results revealed a significant decreased in T3 hormone in groups treated with Xenical drug compared with treated group with mix extract and control groups, also the results show significant increased in T4 hormone in groups treated with Xenical drug compared with plant extract and control group. Statistical analysis showed no significant differences in the TSH hormone among the three groups (Table 3).

AST enzyme level in Xenical group significantly increased compared to the control group and mix plant group. The results also showed a significant increase in the ALT and ALP enzymes of the Xenical group compared with control and group treated with mix extract (Table 4).

B.urea had a significant rise in Xenical group compared to plants extract group and control, while creatinine recorded no significant differences in all treated groups compared to control (Table 5).

Obesity became a worldwide pandemic which require treatment and one of the most common used drug is Xinical. It is a well-known for its efficacy in reducing body weight through improving Metabolism then subsequently improving liver and kidney function (Humayun *et al.,* 2016; Guerciolini *et al.*, 1997). In this study, the body weight was decreased significantly in the treated groups in both xinical (orlistat) and natural plant extract in comparison to control (untreated) group. The main mechanism of orilstat in weight reductionthrough theinhibition of lipase a pancreatic enzyme that catalyze the hydrolysis of lipid which prevent the absorption of lipid in intestine and eventually exerting lipid in feces (Al-Safo *et al.*, 2022).

It is well known that obesity is related to lipid abnormalities, thus the lipid profile were measured and the result indicated a significant decrease in cholesterol, triglyceride, LDL,and VLDL while a statistical increase was shown in HDL in both orlistat and natural plant extract with a lower effect in natural treatment (plant extract) than the drug(orlistat), this result is due to the blocking potential of orlistat to lipase activity which led to the prevention of triglyceride breakdown and excretion of lipid. This will lower the accumulation of lipids and their break down derivative and finallycontrolling one of the main causes of obesity (Eid *et al.*, 2023, Amin *et al.*, 2015).

Decrease in glucose level was found in both treatments in contrast to control. This result proven by (Johan *et al.*, 2022) who estimated HbA1c and fasting plasma glucose and attributed it to the mechanism of xinical which reduce lipid digestion, increase insulin sensitivity, decrease adipose tissue and increase the secretion of glucagon all of these will enhance glycemic control. They mentioned as well that xinical as thyroid hormone are routinely requested when measuring obese status (Filippatos *et al.*, 2008). Thyroidfunction was measured and the result showed that there was no significance variation in TSH which was agreed by (Aydin *et al.*, 2022). While, xinical showed a significant decrease inT3 compared to natural extract and control with opposite result collected in T4 hormone as a statistical elevation found only in xinical. It was found that fat accumulation is related to disturbance of thyroid hormones (high TSH and low T4) and our result elevated T4 which may be a cause

Table 3: Comparison between the effect of Xenical drug and mix plants extract on thyroid hormones in rats.

Groups	T3 ng\dl	T4ug\ml	TSH uIU\ml
Control	80 .34±1.74^{a}	6.32±2.63^{b}	3.68 ±0.43^{a}
Xenical 120 mg\kg	50.43 ±2.86^{b}	12.32±0.56^{a}	2.42 ±0.22^{a}
Mix plant 200 mg\kg	75.34±2.95^{a}	6.32 ±0.96^{b}	3.88 ±0.41^{a}
LSD	6.65	2.09	1.04

Means having with the different letters in same column differed significantly. * (P≤0.05).

Table 4: Comparison between the effect of Xenical drug and mix plants extract on liver function in rats.

Croups	AST IU\L	ALT IU\L	ALP IU\L
Control	26.33±0.88^{B}	30.53±1.45^{b}	103.43±3.86^{c}
Xenical 120 mg\kg	40.43±1.32^{a}	38.40±1.64^{a}	144.33±4.88^{a}
Mix plant 200 mg\kg	29.53±2.54^{B}	32.16±2.70^{b}	124.19±1.95^{b}
LSD	4.03	3.77	5.29

Means having with the different letters in same column differed significantly. * (P≤0.05).

Table 5: Comparison between the effect of Xenical drug and mix plants extract on kidney function.

Groups	B.urea mg\kg	Creatinine mg\kg
Control	25.84±1.54^{B}	0.53±0.03^{a}
Xenical 120 mg\kg	40.93±2.30^{A}	0.61±0.02^{a}
Mix plant 200 mg\kg	27.83±2.62^{B}	0.50±0.04^{a}
LSD	2.85	0.06

Means having with the different letters in same column differed significantly. * (P≤0.05).

for reducing body weight (Hsieh *et al.*, 2005, Sanyal *et al.*, 2016).On the other hand the natural extract did not show an influence on thyroid hormone which may indicate that this material had another mechanism on metabolism.

Kidney function is vital for the life any defect may threat the creature life, one of the determinant of orlistatis their side effect on kidney, as the un-digest able lipid capable to bind with free calcium that should bind to oxalate in intestinal lumen, followed by elevation in oxalate absorption and finally secondary kidney damage due to accumulation of oxalate stones (Nicholls *et al.*, 2001).

Liver function results showed statistical elevation in both ALT and AST enzymes in xinical in compared to control and plant extract, which may indicate a liver injury which consider an agreement with (Youssef *et al.*, 2018) who observed liver cellular inflammation infiltration and necrosis after the treatment with orlistat.

The natural plant extracts including Fennel which contain multiple active components that regulates fat digestion and storage , anise oil that cause decrease in fatty acid , low densitylipoproteins and cholesterol (Ahmed *et al.*, 2022). The green tea acts as thermo genic food and fat oxidation. Carvacrolan active compound in caraway is the main factor related to reduce body weight due to their antioxidant activity and its positive role in gut normal flora which improve digestion (Kazemipoor *et al.*, 2013, Salih *et al.*, 2024, Majda *et al.*, 2022). In concern to coriander which is rich in poly phenolic compound, these compounds was found to increase liver metabolism of cholesterol to bile acid that exerted by fesses and ameliorate obesity(Scandar *et al.*, 2023, Al-Rubaye *et al.*, 2016, Abdul-Jalil *et al.*, 2023).The combination of these compounds may act synergistically to inhabit different enzymes to reduce body weight (Sayed *et al.*, 2023; Yahya *et al.*, 2024).

CONCLUSION

The above result showed that xinical had a higher anti-obesity activity than plant extract , though the side effect of xinical on liver and kidney was higher than the natural product. This may indicate that natural extract of plant is favorable on xinical but require a longer time to work perfectly.

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Authors contributions

All authors are equally contributed in this study.

Ethics

Approval was obtained from Biotechnology Research Center/ Al-Nahrain University of the Animal Health Care Committee under the ethical approval number (E. B. 14) dated (2.1.2023).

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Conflict of interest

The authors have not declared any conflicts of interest.

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