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Research Article
Physiological Effects of Fig Leaf Extract and Orlistat on Obesity, Kidney and Liver of Rats

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Abstract

Background and Objective: Obesity is a global health epidemic associated with various health complications. This study investigates the potential effects of ethanolic fig leaf extract and orlistat on obesity, as well as their impact on kidney and liver function in a rat model, aiming to contribute to the development of strategies for managing obesity-related health issues. **Materials and Methods:** Forty male albino rats with hypercholesterolemia were divided into four groups: Group one served as a control and received a normal diet, group two was a control group that was fed a high-fat diet, group three received a high-fat diet with a daily force-fed ration of 3 g kg^{-1} b.wt., of fig leaves and group four received a high-fat diet along with daily administration of orlistat at 4 mg kg^{-1} b.wt. Blood samples were collected from all groups at baseline and after 30 days of treatment. **Results:** Rats in the high-fat diet group showed a significant increase in body weight by 49%, while rats treated with fig leaf extract showed a significant decrease in body weight by 18% ($p<0.01$) and treatment with orlistat resulted in 12% elevation in body weight. Renal function markers creatinine and urea were decreased in the group treated with fig leaves. Liver enzymes AST, ALT and ALP decreased significantly in the group treated with fig leaves and orlistat. Albumin and globulin concentrations decreased more with fig leaf extract than with orlistat. **Conclusion:** Fig leaves and orlistat reduce body weight and improve kidney and liver function in hypercholesterolemic rats.

Key words: Fig leaves extract, orlistat, liver enzymes, creatinine and obesity

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Fig leaves, scientifically classified as *Ficus carica*, originate from a deciduous tree in the Moraceae family. Obesity is a serious global health problem, characterized by excessive accumulation of fat in the body, with a Body Mass Index (BMI) above 30 indicating obesity. This pathology affects more than half a billion people worldwide and is often associated with various metabolic disorders[1]. The consequences of obesity have reached epidemic proportions, leading to more than 4 million deaths each year[2]. Obesity is a complex disease that increases the risk of many other diseases and health complications, thereby placing a significant economic burden on the health system. Chronic Kidney Disease (CKD) is common in older people and is distinct by structural or functional abnormalities of the kidneys leading to kidney failure accompanied by cardiovascular disease, liver damage and an overall high rate of mortality[3]. The global incidence of CKD is expected to increase by 40% over the next decade. Low- and middle-income countries are experiencing a transition from normal weight to overweight and obesity, mirroring trends seen in many regions in Europe and the United States in recent decades[4]. This increase in obesity prevalence has important implications for cardiovascular and renal health, as high BMI is an important risk factor for the development of chronic kidney disease[5]. Obesity is closely associated with the development of metabolic syndrome (MetS) and comorbidities such as Type 2 Diabetes (T2DM), Non-Alcoholic Fatty Liver Disease (NAFLD) and chronic kidney disease[6,7]. The increasing prevalence and severity of NAFLD is associated with increasing rates of obesity. Therefore, combating obesity is essential to minimizing its adverse effects on several organ systems, including the kidney and liver[8-10]. In the following study, the effect of ethanolic fig leaf extract on the liver and kidney function of rats was examined compared to the orlistat drug.

MATERIALS AND METHODS

Study area: This study was done at The Al al-Bayt University, Al-Mafraq City in Jordan, starting from June, 2023 and finishing in September, 2023.

Extract preparation: Fig leaves were taken from Al Mafraq farm, cleaned and dried at room temperature. Four hundred grams of dried leaves were ground and the extract was obtained by distillation using 70% ethanol (1000 mL) at room temperature for 72 hrs. After filtration, the ethanol was evaporated at 40°C using a rotary evaporator (REV-3000 Series Infitek Company, New York, United States) and the extract was stored at -20°C. The study received approval from the Medical Ethics Committee of Al Al-Bayt University.

Experimental design and animals: Forty male albino rats weighing between 250 and 260 g were obtained from Jordan University of Science and Technology. Rats were fed a hypercholesterolemic diet containing 6% cholesterol, 0.25% bile salts and 20% allowed for two weeks to induce hypercholesterolemia. Subsequently, the rats were divided into four groups, each group consisting of 10 rats. The treatment period lasts 30 days and the groups are as follows:

- **Control group:** Rats received a normal diet
- **High-fat diet control group:** Rats were fed a high-fat diet
- **Group treated with fig leaves:** Rats were fed a high-fat diet and received 3 g kg^{-1} b.wt., of fig leaf extract daily by gavage
- **Group treated with orlistat:** Rats were fed a high-fat diet and received 4 mg kg^{-1} b.wt., of orlistat gavage daily

Biochemical parameters: Throughout the study, the body weight of the rats was monitored and various biochemical parameters related to liver and kidney function were assessed, including liver enzymes (AST, ALT, ALP), liver proteins (albumin, globulin) and renal markers (creatinine, urea) using Enzyme-Linked Immunosorbent Assay (ELISA) Reader from BMG LABTECH company in Offenburg, Germany. After 30 days of treatment, rats were anesthetized after an overnight fast and blood samples were taken by cardiac puncture. Serum samples were obtained by centrifugation at 3000 rpm for 10 min and stored at -20°C until analysis. Analyzes were performed in the Jerusalem Consulting Laboratory (Zarqa, Jordan).

Statistical analysis: Data analysis was performed using SPSS software version 22.0. Results were presented as Mean±Standard Deviation (SD) and statistical significance was determined using the $p<0.05$.

RESULTS

This study aimed to investigate the physiological effects of fig leaves and the drug orlistat on kidney and liver function in obese rats. As shown in Fig. 1, significant increases in body weight were observed in all groups. The control group on a

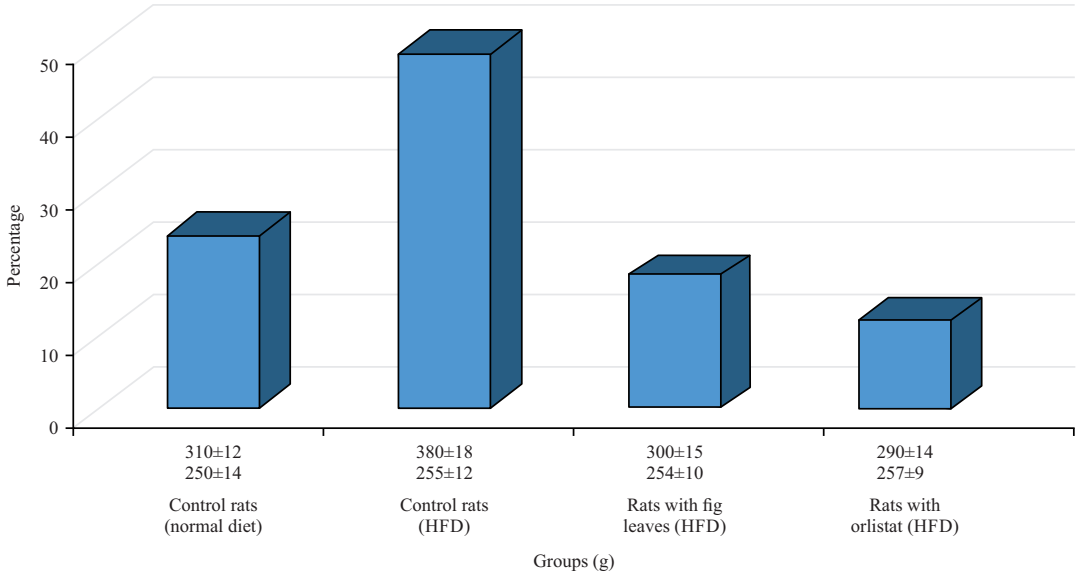

Fig. 1: Effect of fig leaf and orlistat in the body weight (g) in all studied groups (Mean±SD)

Table 1: Effect of fig leaf extract and orlistat on the kidney rats

Group (g)	Creatinine (mg dL^{-1})	Urea (mg dL^{-1})
Control rats (normal diet)	0.3±0.1	17.1±3.6
Control rats (HFD)	0.4±0.2	25.2±2.8
Rats with fig leaves (HFD)	0.3±0.2**	18.6±2.7**
Rats with orlistat (HFD)	0.4±0.1	22.1±2.1*

Measurements of creatinine and urea (Mean±SD), Significance at **p<0.001 and *p<0.05

Table 2: Effect of fig leaf extract and orlistat on the enzymes and proteins of rat liver

Group (g)	AST (μ mL^{-1})	ALT (μ mL^{-1})	ALP (μ mL^{-1})	Albumin (g dL^{-1})	Globulin (g dL^{-1})
Control rats (normal diet)	105.41±13.51	28.62±5.70	113.41±12.50	4.1±0.3	2.1±0.2
Control rats (HFD)	143.41±11.42	47.23±4.62	200.33±13.62	4.8±0.1	2.6±0.1
Rats with fig leaves (HFD)	113.51±6.41*	30.32±5.55**	118.65±10.73**	4.1±0.1**	2.3±0.1*
Rats with orlistat (HFD)	125.53±7.33*	33.12±2.73*	133.54±8.82*	4.5±0.3	2.5±0.1

ALT: Alanine Transaminase, AST: Aspartate Aminotransferase, ALP: Alkaline Phosphatase, HFD: High fat diet, Significant at **p<0.001, *p<0.05 and Mean±SD

normal diet showed a significant increase in body weight by 24% (p<0.05), while the control group on a high-fat diet showed a significant increase in body weight by 49% (p<0.05). In contrast, the group treated with fig leaf extract showed only an 18% increase in body weight and the group treated with orlistat showed a 12% increase. This finding (Fig. 1) highlights the potential of fig leaf extract and orlistat in mitigating the increase in body weight in obese rats, suggesting their role in addressing obesity.

Table 1 shows serum concentrations of renal function markers, creatinine and urea in all study groups. The control group of rats on a high-fat diet showed significantly elevated levels of creatinine and urea. However, treatment with fig leaf extract led to a significant reduction in creatinine and urea concentrations (p<0.001). Orlistat treatment, on the other hand, reduced urea levels but did not significantly affect creatinine levels.

Table 2 shows serum concentrations of liver enzymes (AST, ALT, ALP), as well as liver proteins (albumin, globulin), in all study groups. Control rats on a high-fat diet displayed elevated levels of AST, ALT, ALP, albumin and globulin levels. Treatment with fig leaf extract resulted in a significant reduction at (p<0.001) in the levels of these markers. Similarly, treatment with orlistat also significantly reduced at (p<0.005) the concentrations of liver enzymes and liver proteins.

DISCUSSION

The effect of aqueous fig leaf extract on body weight in addition to liver enzyme and creatinine is well documented. The significant effect of the extract on these parameters was in coincided with previous studies which revealed that fig leaves have been shown to reduce serum total bilirubin, aspartate aminotransferase, malondialdehyde equivalent and

serum alanine transaminase levels, which serve as indicators of hepatic lipid peroxidation[11,12]. Herbal medicines have been used for centuries due to their relatively fewer side effects. Fig leaves are rich in antioxidants that help in free radical elimination[9]. Fig leaves are particularly rich in minerals and have high energy density and fiber content, which may have beneficial effects on weight control[10]. The presence of soluble fiber, minerals, vitamins and various health-promoting phytochemicals in fig leaves may contribute to their role in weight loss and improving overall health. Fiber is known to create a feeling of fullness in the stomach, making it a valuable ingredient in weight loss diets[13,14]. A high-fat diet can lead to increased liver enzyme levels due to oxidative stress and treatment with fig leaf extract significantly reduced these increases, supporting the results of study by Mohammed *et al.*[15]. The hepatoprotective effect of fig leaves may be due to the presence of flavonoids, including quercetin, which have potential hepatoprotective properties[16]. Flavonoids, carotenoids and triterpenes present in fig leaves exhibit antioxidant activity by scavenging reactive oxygen species, thereby preventing potential damage to cellular components such as DNA, proteins and lipids. This protective action extends to hepatocyte cells of the liver[17]. The reduction in kidney markers of creatinine and urea may also be due to the kidney-protective effects of fig leaves, which have been demonstrated in previous studies. Hydroalcoholic extract of *Ficus carica* has been shown to reduce serum urea, creatinine and urea nitrogen concentrations in gentamicin poisoning, showing nephron protective properties[18,19].

CONCLUSION

This study highlights the potential therapeutic effects of fig leaves and orlistat in reducing obesity and improving kidney and liver function in hypercholesterolemic rats. Fig leaves and orlistat significantly reduced body weight, kidney markers and liver enzymes and fig leaf extract showed a more pronounced effect on liver protein levels. These findings highlight the promise of fig leaves as a natural remedy for obesity-related health problems and warrant further research into their clinical applications. Further phytochemical investigation should be focused on the prevalence constituent in fig leaves that contributed to their medicinal value.

SIGNIFICANCE STATEMENT

This study was essential to address the pressing global health issue of obesity and its repercussions on kidney and liver function in hypercholesterolemic conditions. This research aimed to assess the distinctive effects of fig leaf extract and orlistat on these physiological parameters in rats. By demonstrating that fig leaf extract led to a substantial reduction in body weight, alongside improvements in renal and hepatic function, we underscore its potential as a natural intervention for obesity-related complications.

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