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Effect Of Garlic Supplementation On Body Weight When Given Along With Orlistat In High Fat Diet Fed Obese Rats

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Abstract

Background: Obesity is a chronic, multifactorial metabolic disorder characterized by excessive accumulation of body fat that adversely affects health. Many pharmacologic interventions have been developed among which orlistat is one of the most commonly prescribed drug. But evidence suggests that orlistat is not free of adverse effects, which requires adjuvant use of natural supplements for augmented benefits with fewer side effects.

Aims and Objectives: To aim of this study is to determine the effect of garlic supplementation on body weight of high fat diet fed obese rats when given alongside orlistat.

Material and Methods: In this experimental study, 36 male albino rats were assigned into 4 groups having 9 rats each.. Group 1 received normal rat chow diet, Group 2 was fed with high fat diet (HFD) for 14 weeks. Group 3–5 animals were fed with HFD for 8 weeks, after that Group 3 received HFD + Orlistat 32mg/kg and Group 4 was given HFD + Orlistat 32mg/kg + garlic extract 500mg/kg for a period of 6 weeks. Body weight was observed on weekly basis and recorded on 0^{th}, 8^{th} and 14^{th} week. Data was analyzed using SPSS version 27 and results with p-value ≤ 0.05 was considered significant.

Results: Group 4 (orlistat and garlic combined group) exhibited greater weight loss when compared with group 3 (orlistat only group)

Conclusion: Garlic supplementation appears to exert a beneficial modulatory effect on body weight when administered alongside orlistat in experimental rats.

Introduction

In recent years, obesity has emerged as a major global public health concern and is strongly associated with several co-morbid conditions, including diabetes mellitus, cardiovascular diseases, non-alcoholic fatty liver disease (NAFLD), hypertension, and dyslipidemia worldwide[1]. While lifestyle modification and behavioral strategies remain the cornerstone of obesity management, their effects are often limited and difficult to sustain over the long term for many individuals[2]. As a result, pharmacological interventions are commonly employed as an adjunct to lifestyle measures to achieve effective weight control[3].

For this purpose, orlistat emerged as a most commonly prescribed long term weight loss drug[4]. Despite its efficacy in weight loss, prolonged use of orlistat has been associated with undesirable effects, including altered lipid metabolism and hepatic changes. Natural products with antioxidant and lipid-lowering properties have gained attention as potential adjuncts to conventional anti-obesity drugs[5]. Garlic (Allium sativum) is one such medicinal plant that has been extensively studied for its metabolic, antioxidant, and anti-inflammatory effects[6]. The current study was designed to evaluate if combining garlic supplementation with orlistat may enhance therapeutic benefits while minimizing drug-induced adverse effects.

Orlistat exerts its anti-obesity effect by blocking pancreatic and gastric lipases, resulting in decreased intestinal fat absorption[7]. This leads to weight reduction and improvement in certain metabolic parameters. However, impaired fat absorption may also disturb fat-soluble vitamin levels and increase oxidative stress, particularly in hepatic tissue[8]. These effects highlight the need for adjunct therapies that can counteract metabolic and biochemical disturbances associated with long-term orlistat administration.

Garlic contains several biologically active sulfur-containing compounds, including allicin, diallyl disulfide, and S-allyl cysteine[9]. These compounds are known to influence lipid metabolism, glucose homeostasis, and oxidative stress pathways. Garlic supplementation has been reported to reduce body weight gain, improve serum lipid profiles, and enhance antioxidant defense mechanisms in experimental models of obesity[10]. In this study, we want to evaluate whether garlic supplements antiobesity effects exerted by orlistat.

Materials and Methods:

Study Design and Setting:

This experimental study was conducted in the animal house of Akhtar Saeed Medical and Dental College, Lahore after getting reviewed and approved by Ethical committee of Superior University, Lahore.

Study was conducted on 36 male albino rats, weighing 150-200g, 8-10 weeks of age. Rats were initially kept for a period of 2 weeks for acclimatization with room temperature maintained at 24± 2°C with 12 hours of light and 12 hours of darkness to maintain their circadian rhythm.

Drugs and Chemicals:

Orlistat capsule (under trade name abnil) 120mg

Aqueous Garlic extract

The high fat diet prepared by mixing of 68% normal rat chow, 20% instant milk powder, 6% ghee and 6% corn oil[11].

Grouping of animals:

After 2 weeks of acclimatization, rats were divided into 4 groups with 9 rats in each group as follows:

Group 1 - control group receiving distilled water as a daily dose
Group 2- receiving high fat diet(HFD) only
Group 3– HFD and orlistat (32mg/kg/day)[12][13]
Group 4- HFD, orlistat (32 mg/kg) and garlic extract (500mg/kg)[14].
Study was conducted in 2 phases. In the first phase after acclimatization (0-8 weeks), group 1 received normal rat chow diet and distilled water only, while other 3 groups received HFD for induction of obesity. At the end of obesity induction phase, obesity status of the rats was determined by the Lee Index which was calculated based on of the formula described by Lee[15].

$$\text{Lee index\%} = \frac{\sqrt[2]{\text{body weight (g)}}}{\text{naso} - \text{anal length(cm)}} \times 100$$

Rats exhibiting a Lee Index of 310 or higher were classified as obese[14].
In the second phase (9-14 weeks) drugs were administered to group 3 and 4 via oro-gastric lavage for a period of 6 weeks. Body weight was observed on weekly basis and was recorded on 0^{th}, 8^{th} and 14^{th} week.
Data was analysed by SPSS version 27. Data was expressed as mean ±SD and comparison among groups were done by One way Anova and post-hoc tukey's and dunnett's test where required. P-value ≤0.05 was considered significant.

Results:
The body weight of animals was observed on weekly basis throughout experimental period and was recorded at the start of the experiment and subsequently at the 8th and 14th weeks across all study groups (Table 1, Figure 1).

Table 1
Descriptive Statistics of Body Weight (g) at Different Times

Time	Control	HFD	HFD + Orlistat	HFD + Orlistat + Garlic
0 week	156.2 ± 6.3	164.2 ± 3.5	166.0 ± 3.8	168.6 ± 2.5
8th week	191.4 ± 3.5	241.2 ± 4.4	243.1 ± 3.9	237.7 ± 7.4
14th week	212.1 ± 5.1	337.1 ± 8.8	286.1 ± 2.8	259.1 ± 6.8

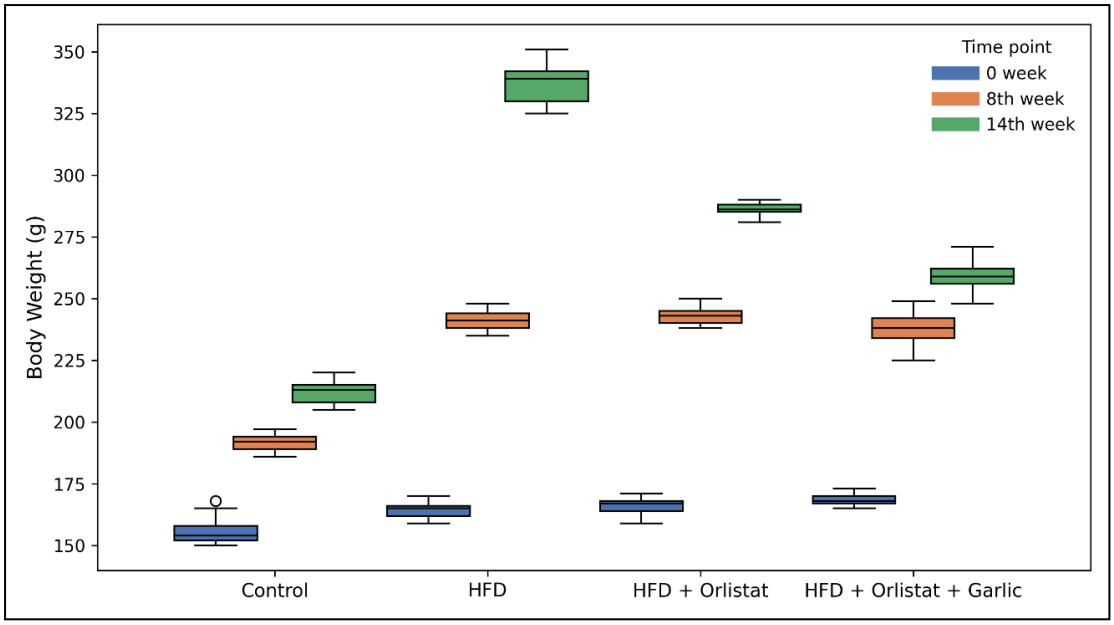

Figure 1: Boxplot Presenting Distribution of Body Weight by Groups at Three Readings

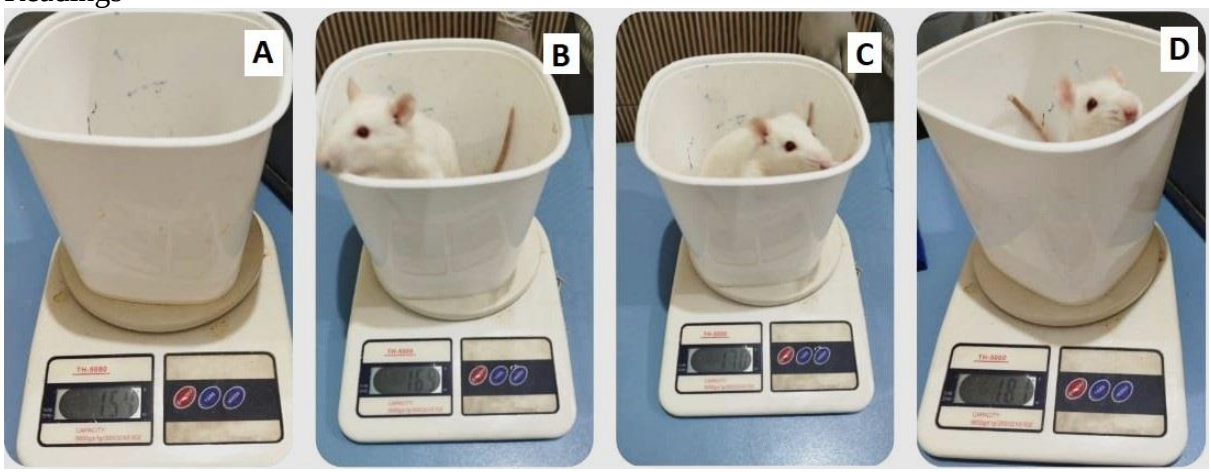

Figure 2: Body weight of rats at 0^{th} week

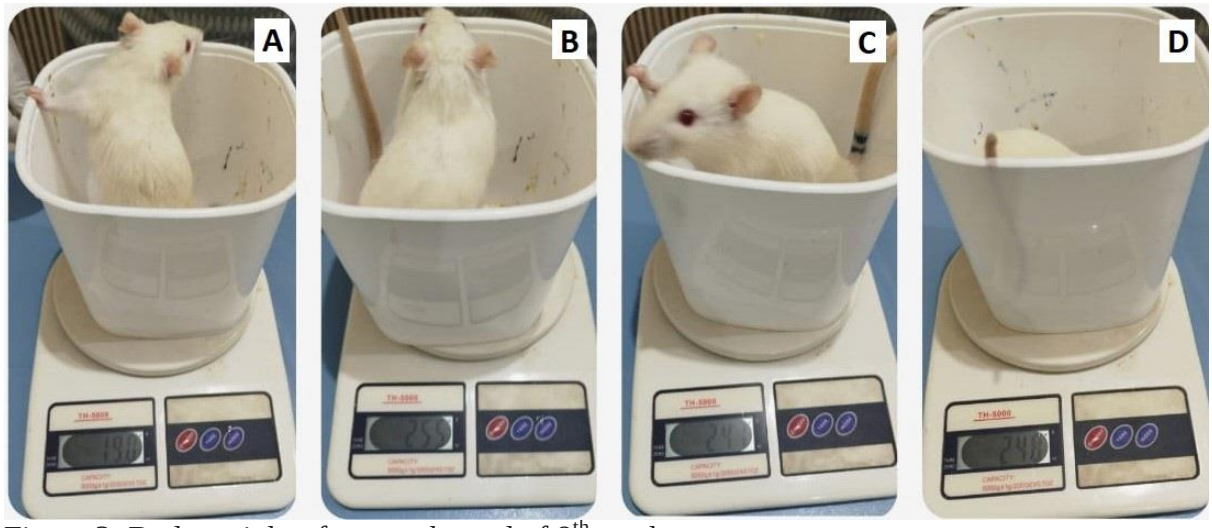

Figure 3: Body weight of rats at the end of 8^{th} week

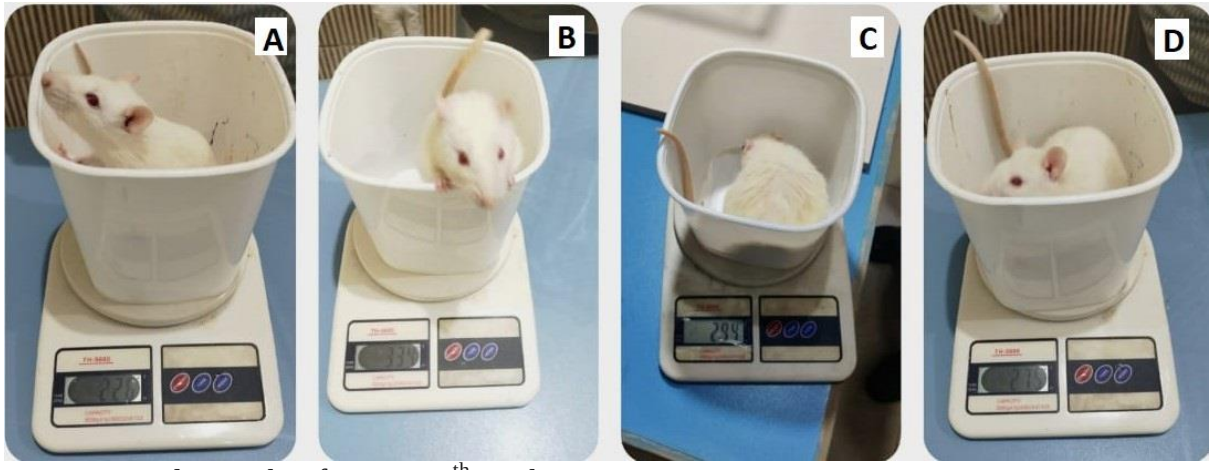

Figure 4: Body weight of rats at 14th week

Where 'A' represents group 1(control group), 'B' represents group 2 (HFD), 'C' represents Group 3(HFD+ orlistat), 'D' represents group 4(HFD+ orlistat+ garlic extract)

At overall comparison made through One-way ANOVA revealed statistically significant differences in body weight among groups at all three time points, including baseline, 8th week, and 14th week with p-values < 0.001 (Table 2).

Table 2 One-Way ANOVA for Body Weight (g) Across Study Groups

Time	Source	Sum of Squares	df	Mean Square	F	p-value
0 week	Between groups	765.42	3	255.14	14.04	<0.001
	Within groups	581.33	32	18.17		
8th week	Between groups	16491.64	3	5497.21	215.93	<0.001
	Within groups	814.67	32	25.46		
14th week	Between groups	73629.00	3	24543.00	625.52	<0.001
	Within groups	1255.56	32	39.24		

Post hoc analysis at baseline and 8th week were performed by Tukey's test while at 14th week was performed by Dunnett's test. At baseline the post hoc analysis indicated that the control group had significantly lower body weight compared to all experimental groups with p-values 0.002, <0.001 and < 0.001. Here the differences among the experimental groups themselves were not statistically significant (Table 3). At the 8th week, the comparisons demonstrated that all experimental groups had significantly higher body weights than the control group with p-values < 0.001. However, no significant differences were observed among the HFD, HFD + Orlistat, and HFD + Orlistat + Garlic groups at this time also (table 3).

Table 3 Tukey's Post-Hoc Test for Body Weight (g)

	(I) Group	**(J) Group**	**Mean Difference (I–J)**	**Std. Error**	**P-value**
0^{th} (T)	Control	HFD	-8.000*	2.009	0.002
	Control	HFD + Orlistat	-9.778*	2.009	<0.001
	Control	HFD + Orlistat + Garlic	-12.333*	2.009	<0.001
	HFD	HFD + Orlistat	-1.778	2.009	0.813
	HFD	HFD + Orlistat + Garlic	-4.333	2.009	0.157
	HFD + Orlistat	HFD + Orlistat + Garlic	-2.556	2.009	0.587
8^{th} (T)	Control	HFD	-49.778*	2.379	<0.001
	Control	HFD + Orlistat	-51.667*	2.379	<0.001
	Control	HFD + Orlistat + Garlic	-46.222*	2.379	<0.001
	HFD	HFD + Orlistat	-1.889	2.379	0.857
	HFD	HFD + Orlistat + Garlic	3.556	2.379	0.452
	HFD + Orlistat	HFD + Orlistat + Garlic	5.444	2.379	0.122
14^{th} (D)	Control	HFD	-125.000*	3.370	<0.001
	Control	HFD + Orlistat	-74.000*	1.936	<0.001
	Control	HFD + Orlistat + Garlic	-47.000*	2.833	<0.001
	HFD	HFD + Orlistat	51.000*	3.068	<0.001
	HFD	HFD + Orlistat + Garlic	78.000*	3.700	<0.001
	HFD + Orlistat	HFD + Orlistat + Garlic	27.000*	2.466	<0.001

D: Dunnett's T3 was used for post hoc analysis because of heterogeneity of variances
T: Tukey's HSD was used for post hoc analysis because of homogeneity of variances
By the 14th week, post hoc analysis showed that the HFD group had significantly higher body weight compared to all other groups with p-values < 0.001. Both the HFD + Orlistat and HFD + Orlistat + Garlic groups exhibited significantly lower body weights compared to the HFD group with p-values < 0.001. Moreover, the HFD + Orlistat + Garlic group had a significantly lower body weight than the HFD + Orlistat group, again with p-value < 0.001, indicating an enhanced effect of combination therapy in reducing diet-induced weight gain (Table 3, Figure 1).

Discussion:

Obesity is a chronic, multifactorial metabolic disorder characterized by excessive accumulation of body fat that adversely affects health. Its prevalence has increased at an alarming rate over recent decades, making it one of the most significant global public health challenges. The rising burden of obesity places substantial strain on healthcare systems and underscores the need for effective preventive and therapeutic strategies. Use of pharmacologic agents are not free of adverse effects, which necessitate the need to explore natural supplements for augmented effect with fewer side effects.

The current study has demonstrated that garlic supplementation, when administered alongside orlistat, results in a more pronounced reduction in body weight compared to orlistat alone. This result is consistent with previous studies where combined administration of garlic and orlistat exhibited greater weight loss in experimental rats[14][3]. Allicin, an active sulfur-containing compound released from crushed Allium sativum, has been shown to increase metabolic activity by stimulating adrenal secretion of adrenaline, thereby enhancing lipolysis, increasing energy expenditure, and promoting body weight reduction[15]. Evidence from experimental studies suggests that garlic influences adipose tissue metabolism, leading to weight loss, and may downregulate the expression of genes involved in adipocyte differentiation and fat accumulation[16]. In addition, garlic has been reported to exert favorable effects on plasma lipid profiles, hepatic enzyme levels, systolic blood pressure, atherosclerotic processes, platelet aggregation, and fibrinolytic activity[17].

Garlic may enhance weight loss by improving lipid utilization, suppressing adipogenesis, and modulating appetite-related pathways[18]. The synergistic action of garlic and orlistat appears to provide better control of body weight without exacerbating drug-related adverse effects.

Garlic compounds also inhibit hepatic cholesterol synthesis, enhance fatty acid oxidation, and reduce lipid peroxidation[19]. Additionally, garlic modulates inflammatory mediators and improves mitochondrial function, which collectively support metabolic homeostasis during pharmacological weight loss therapy.

Conclusion:

Garlic supplementation appears to exert a beneficial modulatory effect on body weight when administered alongside orlistat in experimental rats. These findings suggest that garlic could serve as a valuable adjunct to orlistat therapy in obesity management. However, further experimental and clinical studies are required to establish optimal dosing strategies and long-term safety.

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