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The effect of orlistat in high-fat diet induced-obesity in male albino rats.

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Abstract:

Obesity has been considered a global epidemic that needs immediate prevention and control because it causes slew of physiological, psychological, and social problems. The present study aims to investigate the anti-obesity effect of orlistat in male albino rats and investigate the mechanism of its effect. 30 albino male rats weighing between (150 -180 g) were divided into three groups, as following: G I: control group feed normal diet; G II: male albino rats fed with high fat diet for 12 weeks; G III: male albino rats fed with high fat diet and treated with a daily oral dose of orlistat 50mg/kg/day for 45 days. The administration of a daily HFD to male albino rats for successive 12weeks resulted in obesity that was estimated by calculating BMI and increased levels of serum resistin, leptin , insulin , MDA, pro-inflammatory cytokines , lipid profiles and decreased levels of serum irisin, early signs of fibrosis suggesting the onset of non-alcoholic steatohepatitis (NASH).Orlistat treatment resulted in weight loss and marked improvement in inflammation by decreasing interleukin1-ß, interleukin-6 , MDA levels and increases levels of serum irisin and effectively reduces fat deposition and inflammation in liver tissue. Orlistat is a lipase inhibitor resulted in weight loss via fat absorption inhibition and decreasing the inflammatory responses resulted from obesity.

Key Words: Obesity, Orlistat, oxidative stress, lipid profile, steatohepatitis, insulin, irisin, resistin, interleukin-6, interleukin 1-ß.

1. Introduction:

According to World Health Organization data from 2014, more than 1.9 billion adults are overweight, with 600 million of them obese (1). Obesity has been considered a global epidemic that needs immediate prevention and control (2). because it causes not only aesthetic problems, but also abnormal physiological metabolism, which leads to a slew of physiological, psychological, and social problems (3).

It is caused by an imbalance between energy intake and expenditure. The imbalance causes abnormal weight gain and increases the risk of chronic illnesses such as heart disease, cancer, and diabetes (1).

Obesity is still a prevalent and a common health problem, despite the growing awareness of the importance of an active lifestyle and a healthy diet (4).

Orlistat is a treatment option for obese patients with or without type 2 diabetes, as well as for obese patients with metabolic syndrome, associated comorbidities, or concomitant disorders. Orlistat works by covalently attaching to the serine residue in the active site of gastric and pancreatic lipases. When combined with fat-containing foods, orlistat partially inhibits triglyceride hydrolysis, reducing subsequent absorption of mono-acylglycerides and free fatty acids (5).

2. Materials and Methods:

2.1. Animal and Dose Preparation:

2.1.1. Animal:

30 healthy male adult albino rats weighing 200–270 g was purchased from Qassim University College of Agriculture. All rats were housed in cages of 5 rats per cage under standard laboratory conditions (19-25°C, 12 hours); light/dark cycles and a relative humidity of 50–60%. respectively for one week for adaptation to laboratory conditions. Fresh tap water and standard rodent pellets were always available.

2.1.2. Induction of obesity:

Rats has been fed high fat diet then the weight and nose-anus length of each rat of both control and obese groups were measured at the start and at the end of 12 weeks. BMI was estimated by dividing the weight (g) by the square of the nose-anus length (cm2). Animals with BMI greater than 0.68 g/cm2 will be considered obese (6).

$$\textbf{Body mass index (BMI)} = \frac{\textbf{body weight (g)}}{\textbf{Nose-anus length (cm}^{2)}}$$

2.1.3. preparation of high fat diet:

The diet is prepared by mixing (46%) fat [25.5 % corn oil and 20.5% beef tallow or camel lard), 24% carbohydrates, 20.3% proteins, 5% Fiber, 3.7% salt mixture, and 1% vitamin mixture (7).

2.2. Experimental Design:

30 adult male albino rats were arranged into four groups:

Group I: control group feed normal diet.

Group II: Male albino rats fed with high fat diet (7).

Group III: Male albino rats fed with high fat diet (7) and treated with a daily oral dose of orlistat 50mg/kg/day for 45 days (8).

At the end of the study, rats fastened for 24 hours then blood was drawn from the animals by cervical dislocation after anasethia. Sera separated, aliquoted and kept at -80C until used, samples from liver were cut for histopathological analysis and kept at 10% formalin.

2.3. Analytical procedure:

Serum levels of MDA were estimated colorimetrically, while irsin, leptin, insulin, resistin, pro-inflammatory cytokines were estimated by using ELISA technique (48 well plate), all kits 'MyBioSource'

were purchased from Ejadah Trading Corporation for Scientific and Laboratory Equipment, while serum lipid profile was measured at (Lab of kink Fahad Hospital-Riyadh).

2.4. Statistics:

Comparisons between means were carried out using one-way analysis of variance (ANOVA) followed by post hock (Tukey)and the Statistical Analysis System's General Linear Model Procedure (SAS 1982). Multiple comparisons test at $p \leq 0.01$ according to previous (9). This was carried out using Statistical Analysis System (SAS) program software; copyright©1998 by SAS institute Inc., Cary, North Carolina, USA.

3. Results and discussion:

Data from table no.1 and fig.1 revealed that increasing the conc. of orlistat increases the degree of lipase inhibition which is the key enzyme in controlling obesity. These results emphasize the fact that orlistat is a pharmacological agent that used primarily for weight management by inhibiting pancreatic lipase, which reduces dietary fat absorption in the intestine. This mechanism affects not only lipid metabolism but also the body's oxidative stress levels. Inhibiting fat absorption reduces circulating triglycerides and cholesterol, which can affect a variety of metabolic pathways and oxidative stress markers (10).

Figure (1`):Percentage of inhibition of lipase activity of orlistat :

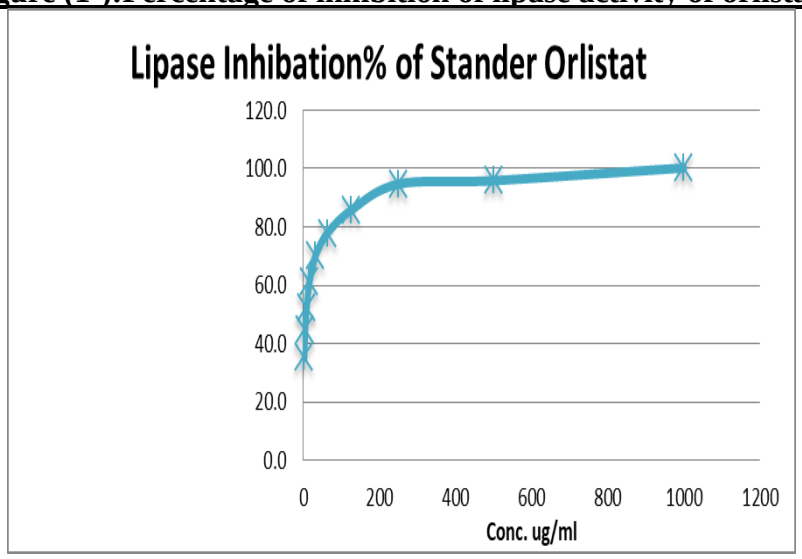

Table (2):Mean value of serum levels of Irisin, Leptin, Resistin and Insulin of control, HFD, and HFD+Orli -treated groups.

Parameters / Groups		Irisin (ng/mL)	Leptin (ng/mL)	Resistin (pg/mL)	Insulin (mlU/L)
Control	M ±SE	4.34±0.10^{A}	1.33±0.03^{A}	230.40±0.06^{A}	42.80±0.09^{A}
HFD		2.10±0.07^{B}	3.37±0.02^{B}	413.60±0.08^{B}	67.60±0.1^{B}
	% Change A	-51.6%	153.4%	79.5%	57.9%
HFD+Orli	M ±SE	3.55±0.03^{C}	2.99±0.05^{C}	334.40±0.02^{C}	49.80±0.06^{C}
	% Change A	69.05%	-11.3%	-19.14%	-26.3%

Data are presented as mean ± standard error of mean. Data were subjected to one-way ANOVA followed by Duncan post hoc test at p≤0.05. Within the same column, means with different superscript letters are significantly different. Orli (orlistat).

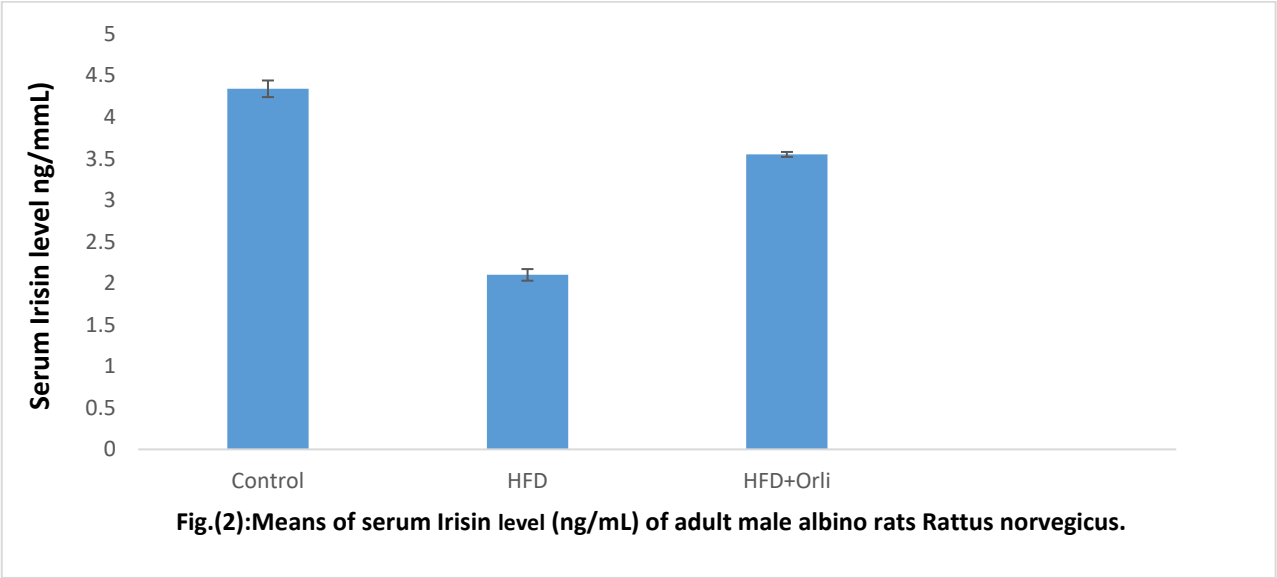

Fig.(2):Means of serum Irisin level (ng/mL) of adult male albino rats Rattus norvegicus.

Serum Irisin level (pg/ml) of adult male Wistar albino rats (*Rattus norvegicus*):

The obtained data in table 2 & figure 2` showed that administration of a daily HFD to adult male rats for 12 consecutive weeks resulted in a significant decline in the levels of serum irisin (-51.6%) by comparing these data with the corresponding values of the control animals' group (2.10 vs 4.34 respectively).

The daily oral administration of orlistat (50mg/kg b.wt./day) for 45 days resulted in a significant improvement (69.05%) in the levels of serum irisin (3.55 vs 2.10) when was compared to the corresponding values of the HFD-treated animals' group. Results of this study are in accordance with other studies as they declared that to the reduction in body fat caused by orlistat treatment may have an impact on the regulation of hormones and metabolic pathways, particularly those involving irisin, a myokine

involved in the browning of white adipose tissue and increased energy expenditure. Irisin is produced by cleavage of the FNDC5 protein and has been shown to promote the conversion of white fat into brown fat, a process known as "browning," which increases thermogenesis and energy expenditure (11-12).
According to studies, circulating irisin levels are positively correlated with metabolic health, with higher irisin concentrations being associated with improved glucose metabolism and insulin sensitivity (13-14). The relationship between orlistat-induced weight loss and irisin levels is particularly interesting because body fat loss may influence irisin secretion. Weight loss interventions, for example, have been linked to increased irisin levels, implying that orlistat's metabolic benefits may be mediated, at least in part, by irisin concentration changes (13-15). Weight loss has been shown in studies to alter FNDC5 gene expression and subsequent irisin release (15). In particular, studies have found that people who lose a lot of weight have higher levels of irisin, which may contribute to the observed improvements in metabolic parameters. In contrast, some studies suggest that reductions in body fat may not always correlate with increased irisin levels, indicating a complex interaction between fat mass, muscle mass, and irisin secretion (11-16)
This complexity is emphasized by the discovery that irisin levels can be influenced by factors such as exercise, dietary patterns, and overall metabolic health (16-18).

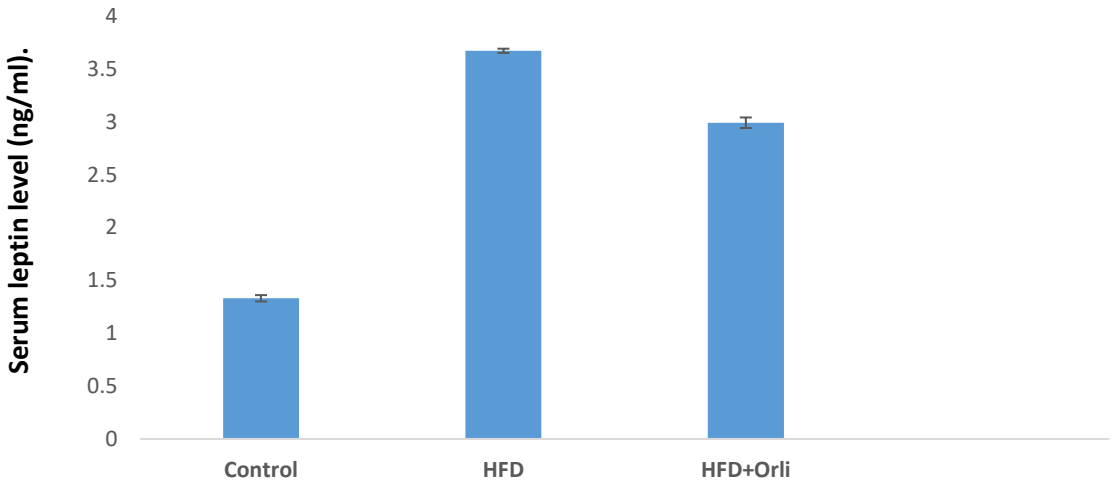

Fig.(3`):means of serum Leptin (ng/ml) of adult male albino rats *Rattus norvegicus.*

Serum Leptin level (ng/mL) of adult male Wistar albino rats (*Rattus norvegicus):*

The obtained data in table 2 & figure 3` showed that treatment of healthy rats with a daily HFD for 12 consecutive weeks resulted in a significant rise in the levels of serum leptin (153.4%), by comparing these data with the corresponding values of the control animals' group (3.37 vs 1.33 respectively).

While the treatment of orlistat (50mg/kg b.wt./day) for 45 days by gavage resulted in a significant decrease (-11.3%) of the elevated levels of serum leptin (2.99 vs 3.37) when was compared to the corresponding values of the HFD-treated animals' group. These results are in accordance with that of a study in 2019 that was attributed to that adipose tissue produces leptin, a hormone that regulates hunger and energy expenditure. A decrease in leptin levels can cause increased hunger and a decrease in resting metabolic rate (RMR), complicating weight management efforts. Leptin levels typically fall as fat mass decreases as a result of losing weight (19).

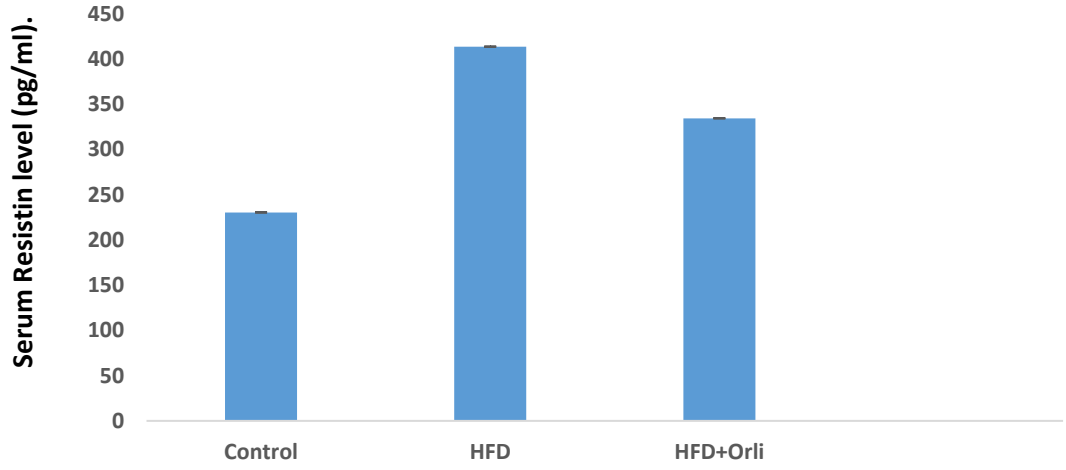

Fig.(4`):Means of serum Resistin level (pg/mL) of adult male albino rats *Rattus norvegicus*.

Serum Resistin level (Pg/mL) of adult male Wistar albino rats (*Rattus norvegicus):*

The obtained data in table 2 & figure 4` showed that treatment of male albino rats with a daily HFD for 12 consecutive weeks resulted in a significant elevation in the levels of serum resistin (79.5%), by comparing these data with the corresponding values of the control animals' group (413.60 vs 230.4 respectively).

On the contrary, the oral injection of HFD-treated rats with orlistat (50mg/kg b.wt./day) for 45 days resulted in a significant decline (-19.14%) of the elevated levels of serum resistin (334.40 vs 413.60) when was compared to the corresponding values of the HFD-treated animals' group. These results are in agreement with many researchers as they mentioned that resistin, is an adipokine secreted by adipose tissue, has been linked to obesity, insulin resistance, and inflammation (20). Resistin levels decrease with weight loss, implying a possible link between weight management and adipokine regulation.

Orlistat, a lipase inhibitor used to treat obesity, may play an important role in this context by promoting weight loss, which could indirectly lower resistin levels and improve insulin sensitivity (21-22).

The link between resistin and orlistat primarily arises from the drug's effects on body weight and fat metabolism. As orlistat promotes weight loss by inhibiting the absorption of dietary fats, it may indirectly contribute to a reduction in resistin production from adipocytes. This suggests that resistin does more than just reflect obesity; it also actively contributes to metabolic dysfunction. In this regard, lowering resistin levels through weight loss interventions, such as orlistat, has the potential to improve insulin resistance and associated inflammatory states.

Resistin levels affect inflammatory markers associated with obesity, including TNF-α and IL-6. Orlistat administration has been shown to reduce these inflammatory markers, implying a dual mechanism in which orlistat aids in weight loss while also mitigating the inflammatory responses associated with obesity (9). This reduction in inflammation, combined with lower resistin levels, may help obese people achieve better metabolic outcomes.

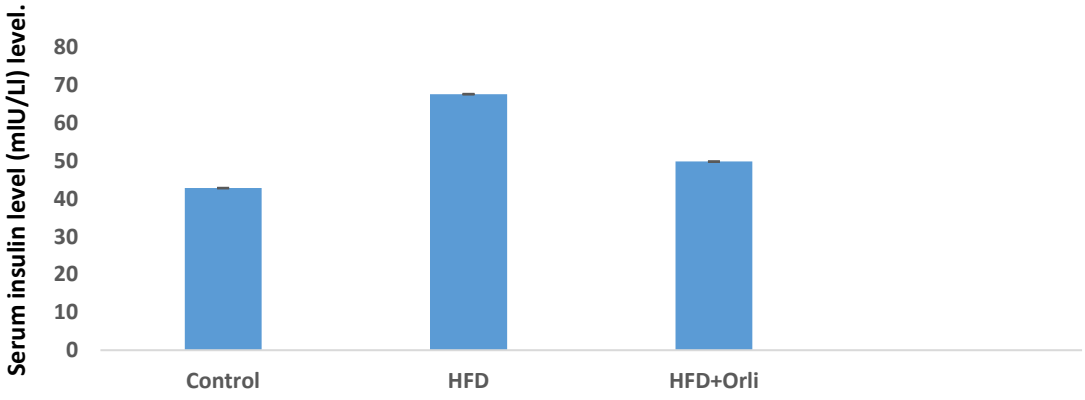

Fig.(5`):Means of serum Insulin level (mlU/L) of adult male albino rats *Rattus norvegicus.*

Serum Insulin level (mlU/L) of adult male Wistar albino rats (*Rattus norvegicus):*

The obtained data in table 2 & figure 5` showed that treatment of male albino rats with a daily HFD for 12 consecutive weeks resulted in a significant elevation in the levels of serum resistin (79.5%), by comparing these data with the corresponding values of the control animals' group (413.60 vs 230.4 respectively).

On the contrary, the oral injection of HFD-treated rats with orlistat (50mg/kg b.wt./day) for 45 days resulted in a significant decline (-19.14%) of the elevated levels of serum resistin (334.40 vs 413.60) when

was compared to the corresponding values of the HFD-treated animals' group. These results may be attributed to that Orlistat, is a lipase inhibitor used to treat obesity, may play an important role in this context by promoting weight loss, which could indirectly lower resistin levels and improve insulin sensitivity (21-22). This mechanism reduces body fat, especially visceral adipose tissue (VAT), leading to metabolic benefits such as improved glycemic control and lower cardiovascular risk factors in both diabetic and non-diabetic populations (23-24).

Table (3):Mean value of serum levels of pro-inflammatory cytokines and Malondialdehyde of HFD, HFD+Orli - treated groups.

Parameters / Groups		IL-1ß (ng/mL)	IL-6 (ng/L)	MDA (nmol/mL)
Control	M ±SE	7.52±0.2^{A}	21.60±0.01^{A}	23.60±0.2^{A}
HFD	M ±SE	18±0.3^{B}	42.40±0.07^{B}	46±0.1^{B}
	% Change A	**139.4%**	**96.3%**	**94.9%**
HFD+Orli	M ±SE	11.75±0.5^{C}	31.00±0.03^{C}	32.40±0.2^{C}
	% Change A	**-34.7%**	**-26.9%**	**-29.6%**

Data are presented as mean ± standard error of mean. Data were subjected to one-way ANOVA followed by Duncan post hoc test at p≤0.05. Within the same column, means with different superscript letters are significantly different. Orli (orlistat).

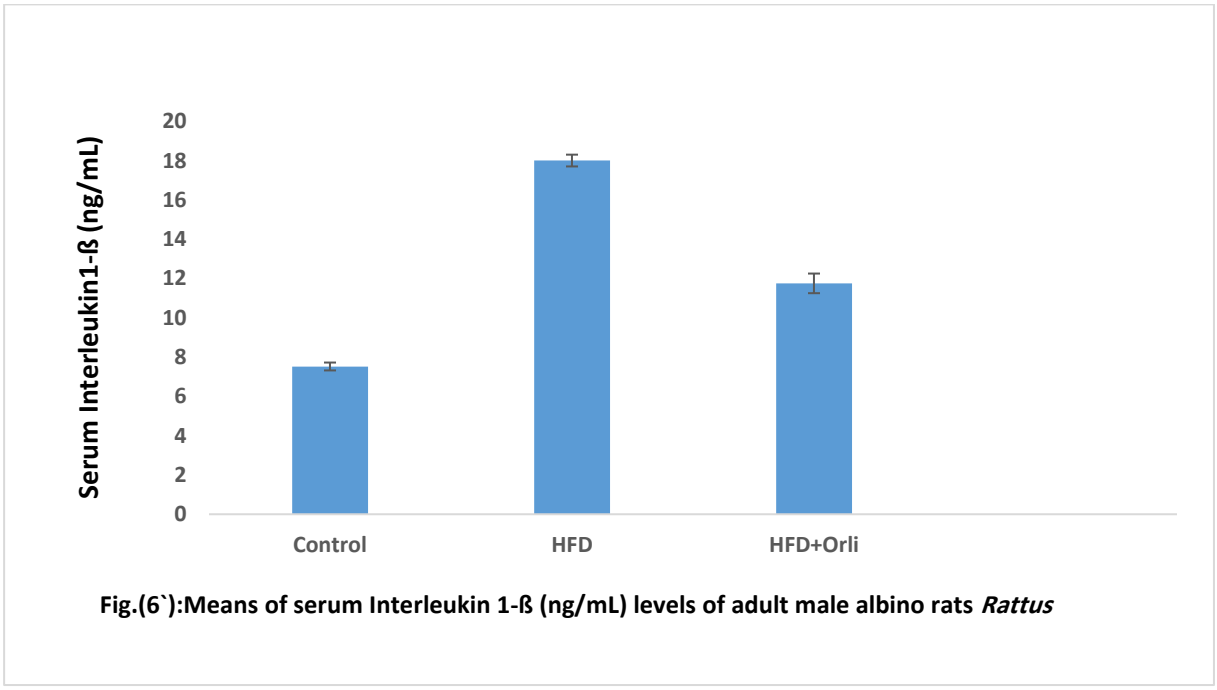

Fig.(6`):Means of serum Interleukin 1-ß (ng/mL) levels of adult male albino rats *Rattus*

Serum Interleukin-1ß level (ng/mL) of adult male Wistar albino rats (*Rattus norvegicus*):

The obtained data in table 3 & figure 6` showed that treatment of male albino rats with a daily HFD for 12 consecutive weeks resulted in a significant rise in the levels of serum **IL-1ß** (139.4%), by comparing these data with the corresponding values of the control animals' group (18 vs 7.52 respectively).

While, the oral treatment of HFD-treated rats with orlistat (50mg/kg b.wt./day) for 45 days resulted in a significant decline (-34.7%) of the elevated levels of serum **IL-1ß** (11.75 vs 18) when was compared to the corresponding values of the HFD-treated animals' group.

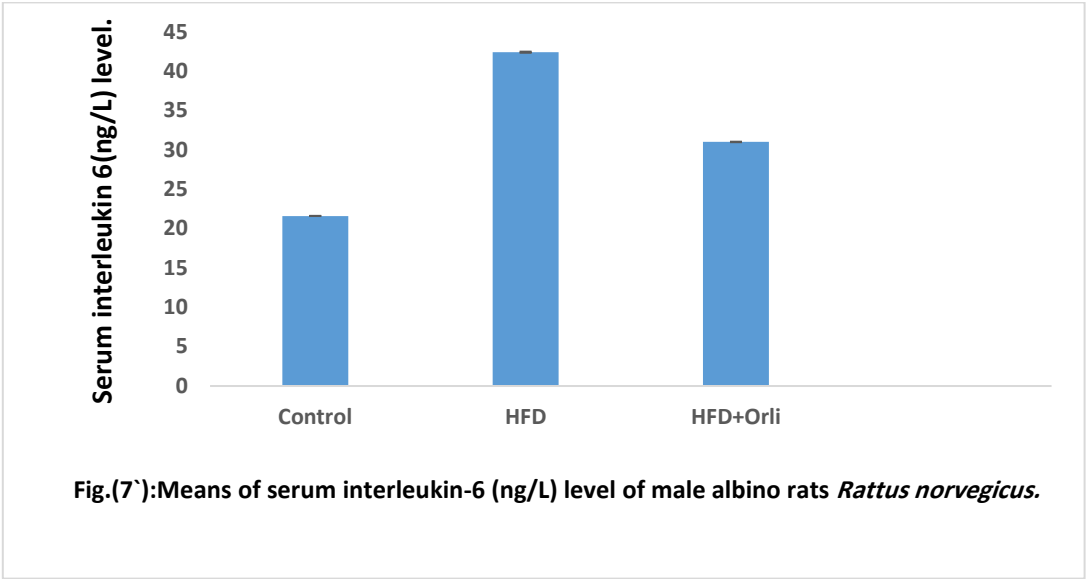

Fig.(7`):Means of serum interleukin-6 (ng/L) level of male albino rats *Rattus norvegicus.*

Serum Interleukin-6 level (ng/L) of adult male Wistar albino rats (*Rattus norvegicus*):

The obtained data in table 3 & figure 7` showed that administration of a daily HFD to male albino rats for 12 consecutive weeks resulted in a significant rise in the levels of serum **IL-6**(96.3%), by comparing these data with the corresponding values of the control animals' group (42.40 vs 21.60 respectively).

While, the oral injection of orlistat to the HFD-treated rats (50mg/kg b.wt./day) for 45 days resulted in a significant decline (-26.9%) of the elevated levels of serum **IL-6** (31 vs 42.40) when was compared to the corresponding values of the HFD-treated animals' group.

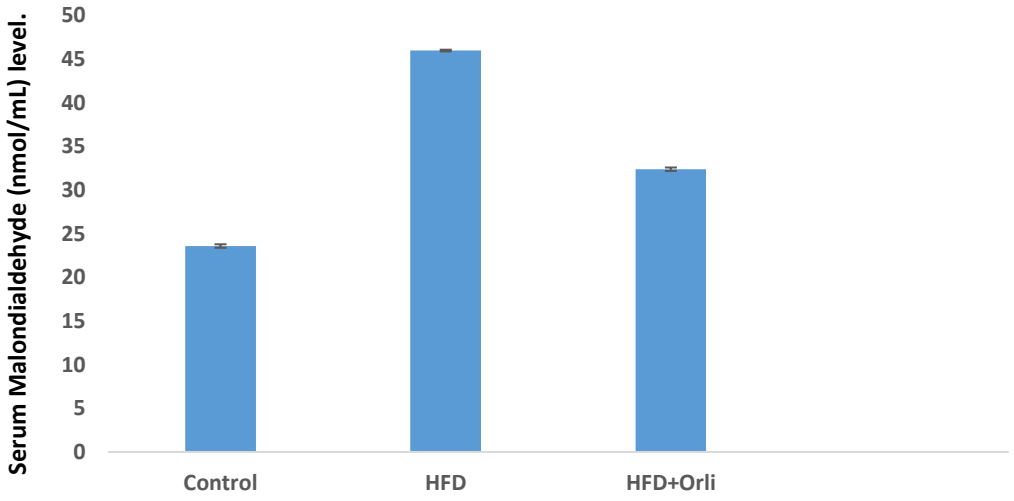

Fig.(8`):Means of serum Malondialdehyde (nmol/mL) of adult male albino rats *Rattus norvegicus*.

The link between orlistat and interleukins, specifically IL-6 and IL-1β, is primarily related to the drug's ability to promote weight loss and reduce fat absorption. Orlistat is a lipase inhibitor that reduces dietary fat absorption, leading to weight loss and visceral fat reduction (24-23). Reducing body fat is crucial as visceral fat secretes pro-inflammatory cytokines like IL-6 and IL-1β, which contribute to systemic inflammation and insulin resistance. According to a research at 2022, losing weight can reduce the levels of these inflammatory cytokines. For example, a study at 2011 found that orlistat treatment resulted in significant improvements in metabolic parameters, including reductions in inflammatory markers associated with obesity. As orlistat may reduce systemic inflammation by lowering IL-6 and IL-1β secretion, as it promotes weight loss (25). High levels of IL-6 and IL-1β have been linked to insulin resistance and metabolic disorders (26). Further research is needed to understand the specific mechanisms by which orlistat affects interleukin levels, as well as the broader implications for inflammation and metabolic health (25-26). Orlistat's ability to promote weight loss and reduce fat absorption likely contributes to a decrease in pro-inflammatory interleukins such as IL-6 and IL-1β. This reduction in inflammatory cytokines may improve insulin sensitivity and lower the risk of metabolic disorders, increasing orlistat's overall effectiveness in treating obesity and related conditions.

Serum Malondialdehyde level (ng/L) of adult male Wistar albino rats (*Rattus norvegicus*):

The obtained data in table 3 & figure 8` showed that administration of a daily HFD to male albino rats for 12 consecutive weeks resulted in a significant rise in the levels of serum **MDA** (94.9%), by comparing these data with the corresponding values of the control animals' group (46 vs 23.60 respectively). While, the oral injection of orlistat to the HFD-treated rats (50mg/kg b.wt./day) for 45 days resulted in a significant

decline (-29.6%) of the elevated levels of serum **MDA** (32.40 vs 46) when was compared to the corresponding values of the HFD-treated animals' group these findings are in line with two studies at 2021; they found that orlistat administration in a high-fat diet-induced metabolic syndrome model significantly reduced oxidative stress markers, implying a protective role against oxidative damage (10-26).

However, the link between orlistat and oxidative stress is complex. Although some studies suggest that orlistat can boost antioxidant defenses, others show that it can cause oxidative stress under certain conditions. A study in 2013 found that orlistat could indirectly improve psychomotor performance by reducing reactive nitrogen species which are frequently linked to oxidative stress (28). This duality suggests that, while orlistat can reduce oxidative stress by inhibiting lipid absorption, it may also contribute to oxidative stress under certain metabolic conditions.

Table (4):Mean value of serum levels of lipid profile of HFD, HFD+Orli - treated groups.

Parameters / Groups		Total-Chol. (mmol/L)	Trigly. (mmol/L)	HDL-Chol. (mmol/L)	LDL-Chol. (mmol/L)
Control	M ±SE	2.50±0.09^{A}	0.96±0.01^{A}	1.39±0.02^{A}	0.67±0.01^{A}
HFD		4.60±0.07^{B}	1.96±0.05^{B}	0.97±0.01^{B}	2.73±0.09^{B}
	% Change A	**84%**	**104%**	**-30.2%**	**307%**
HFD+Orli	M ±SE	3.30±0.07^{C}	1.47±0.07^{C}	1.18±0.02^{C}	1.45±0.07^{B}
	% Change A	**-28.3%**	**-25%**	**%21.6**	**-46.9%**

Data are presented as mean ± standard error of mean. Data were subjected to one-way ANOVA followed by Duncan post hoc test at p≤0.05. Within the same column, means with different superscript letters are significantly different. Orli (orlistat).

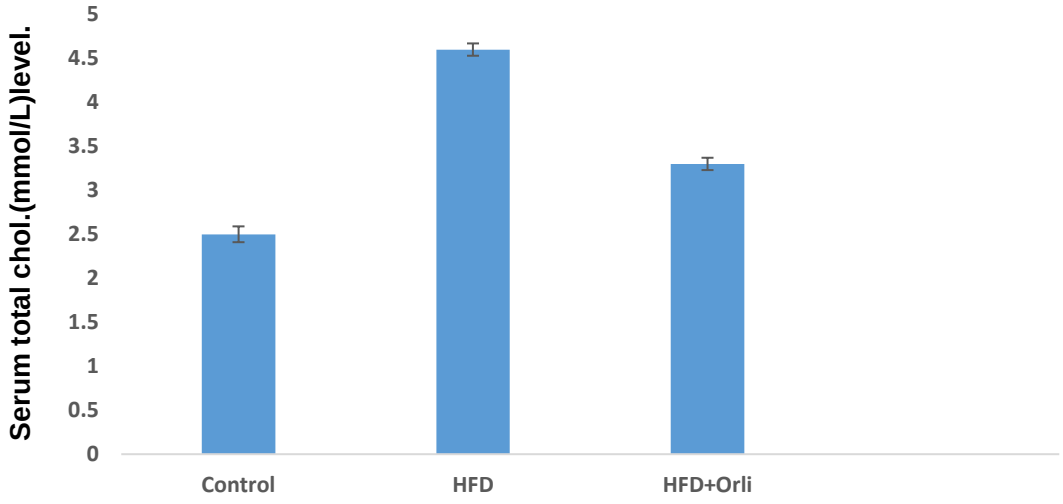

Fig.(9`):Means of serum total Chol.(mmol/L) of adult male albino rats *Rattus norvegicus.*

Serum Total-Chol. level (mmol/L) of adult male Wistar albino rats (*Rattus norvegicus):*

The obtained data in table 4 & figure 9` showed that administration of a daily HFD to male albino rats for 12 consecutive weeks resulted in a significant increase in the levels of serum **total cholesterol** (84%), by comparing these data with the corresponding values of the control animals' group (4.60 vs 2.50 respectively).

On the contrary, the administration of orlistat to the HFD-treated rats by gavage (50mg/kg b.wt./day) for 45 days resulted in a significant decline (-28.3%) of the elevated levels of serum **total cholesterol** (3.30 vs 4.60) when was compared to the corresponding values of the HFD-treated animals' group.

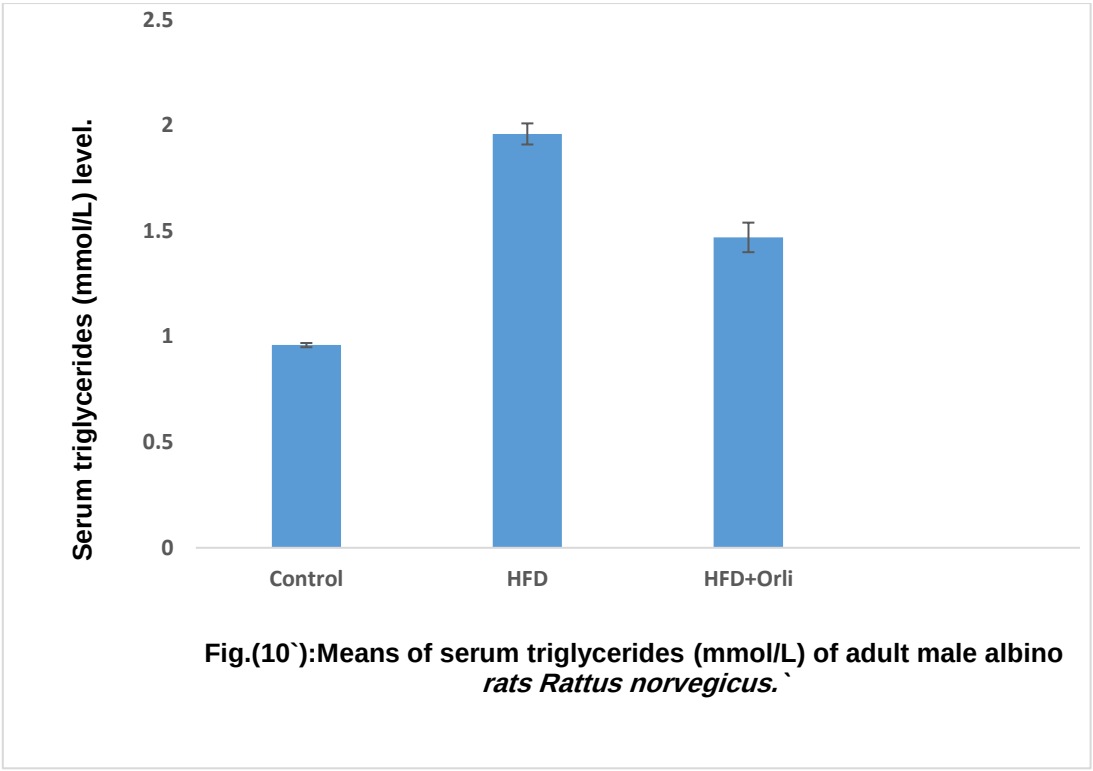

Fig.(10`):Means of serum triglycerides (mmol/L) of adult male albino *rats Rattus norvegicus.`*

Serum Triglycerides level (mmol/L) of adult male Wistar albino rats (*Rattus norvegicus):*

The obtained data in table 4 & figure 10` showed that administration of a daily HFD to male albino rats for 12 consecutive weeks resulted in a significant increase in the levels of serum **triglycerides** (104%), by comparing these data with the corresponding values of the control animals' group (1.96 vs 0.96 respectively).

On the contrary, the administration of orlistat to the HFD-treated rats by gavage (50mg/kg b.wt./day) for 45 days resulted in a significant decline (-25%) of the elevated levels of serum **triglycerides** (1.47 vs 1.96) when was compared to the corresponding values of the HFD-treated animals' group.

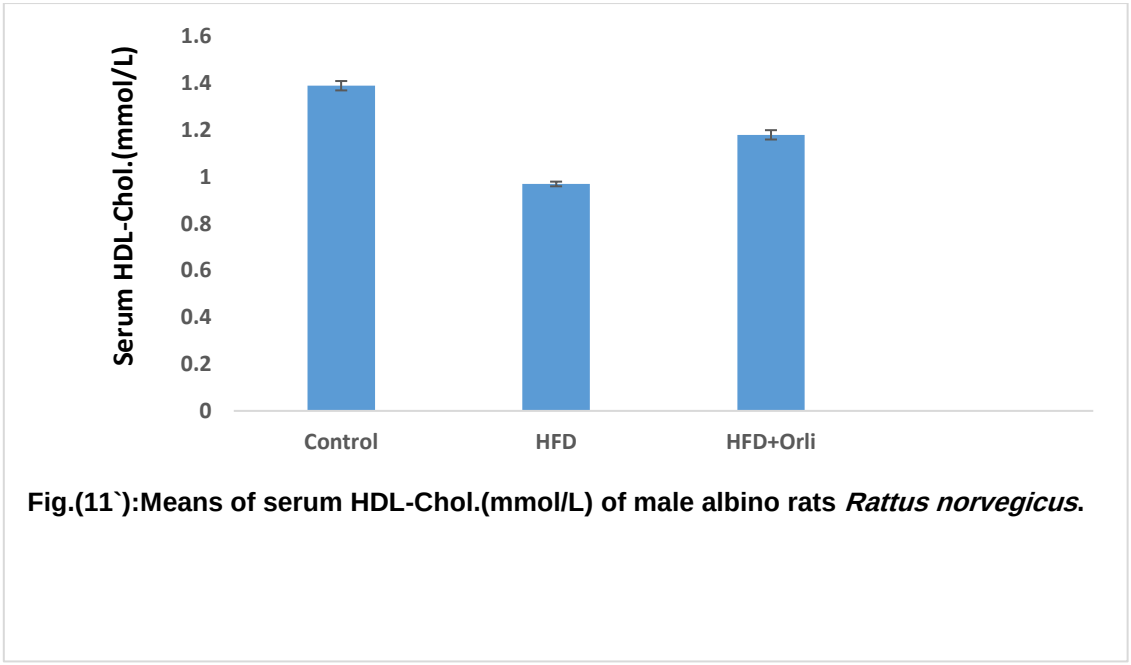

Fig.(11`):Means of serum HDL-Chol.(mmol/L) of male albino rats *Rattus norvegicus*.

Serum HDL-Chol. level (mmol/L) of adult male Wistar albino rats (*Rattus norvegicus*):

The obtained data in table 4 & figure 11` showed that administration of a daily HFD to male albino rats for 12 consecutive weeks resulted in a significant increase in the levels of serum **HDL-Chol.** (-30.2%), by comparing these data with the corresponding values of the control animals' group (0.97 vs 1.39 respectively).

On the contrary, the administration of orlistat to the HFD-treated rats by gavage (50mg/kg b.wt./day) for 45 days resulted in a significant improvement (21.6%) of the declined levels of serum **HDL-Chol. (**1.18 vs 0.97) when was compared to the corresponding values of the HFD-treated animals' group.

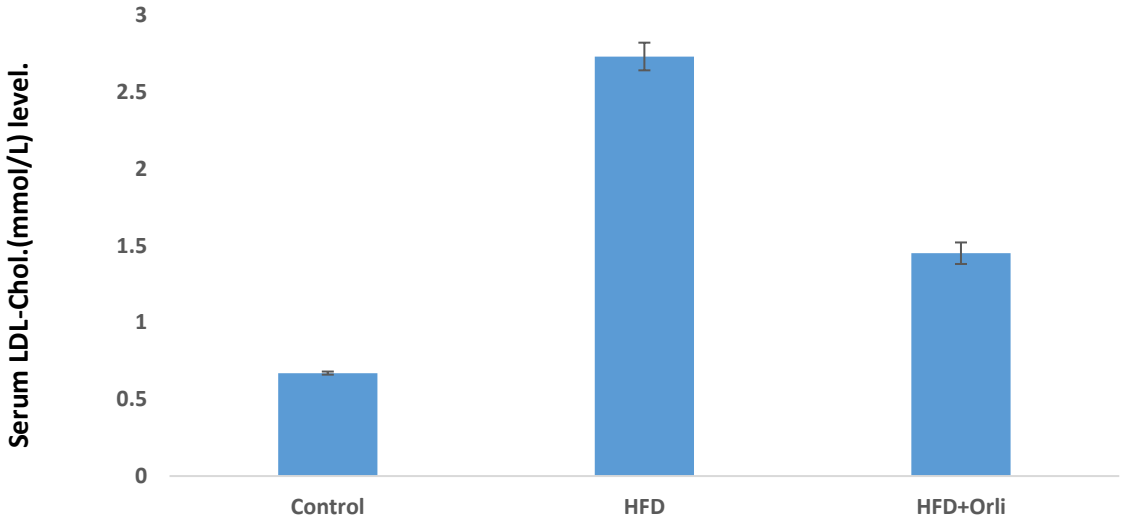

Fig.(12`):Means of serum LDL-Chol.(mmol/L) of adult male albino rats *Rattus norvegicus*.

Serum LDL-Chol. level (mmol/L) of adult male Wistar albino rats (*Rattus norvegicus):*

The obtained data in table 4 & figure 12` showed that administration of a daily HFD to male albino rats for 12 consecutive weeks resulted in a significant increase in the levels of serum **LDL-Chol.** (307 %), by comparing these data with the corresponding values of the control animals' group (2.73 vs 0.67 respectively).

While, the administration of orlistat to the HFD-treated rats by gavage (50mg/kg b.wt./day) for 45 days resulted in a significant decline (-46.9%) of the increased levels of serum **LDL-Chol. (**1.45 vs 2.73) when was compared to the corresponding values of the HFD-treated animals' group. The physiological results are in line with that of histology as shown in table 5, as administration of daily HFD induced widespread macro-vesicular steatosis with large lipid vacuoles pushing hepatocyte nuclei to the periphery. Some hepatocytes appeared ballooned, and sinusoidal spaces were compressed. Mild inflammatory cell infiltration, mainly lymphocytes and macrophages, was noted around portal triads, with early signs of fibrosis suggesting the onset of non-alcoholic steatohepatitis (NASH). The oral injection with orlistat by gavage showed moderate improvement compared to the untreated group. There was reduced lipid droplet accumulation in hepatocytes and less ballooning, with better preservation of hepatic architecture. Inflammatory cell infiltration decreased significantly, and fibrotic changes were minimal. Portal areas remained largely normal, with only mild inflammation and no fibrosis progression. This suggests that Orlistat effectively reduces fat deposition and inflammation in liver tissue.

These results are in harmony with that of previous study in 2021 that reported that orlistat has been shown to effectively reduce dietary fat absorption, which is associated with lower total cholesterol and triglyceride levels in the plasma. This reduction in lipid levels may alleviate some of the oxidative stress associated with high-fat diets (19). Orlistat is a pharmacological agent that used primarily for weight management by inhibiting pancreatic lipase, which reduces dietary fat absorption in the intestine. This mechanism affects not only lipid metabolism but also the body's oxidative stress levels. Inhibiting fat absorption reduces circulating triglycerides and cholesterol, which can affect a variety of metabolic pathways and oxidative stress markers (10).

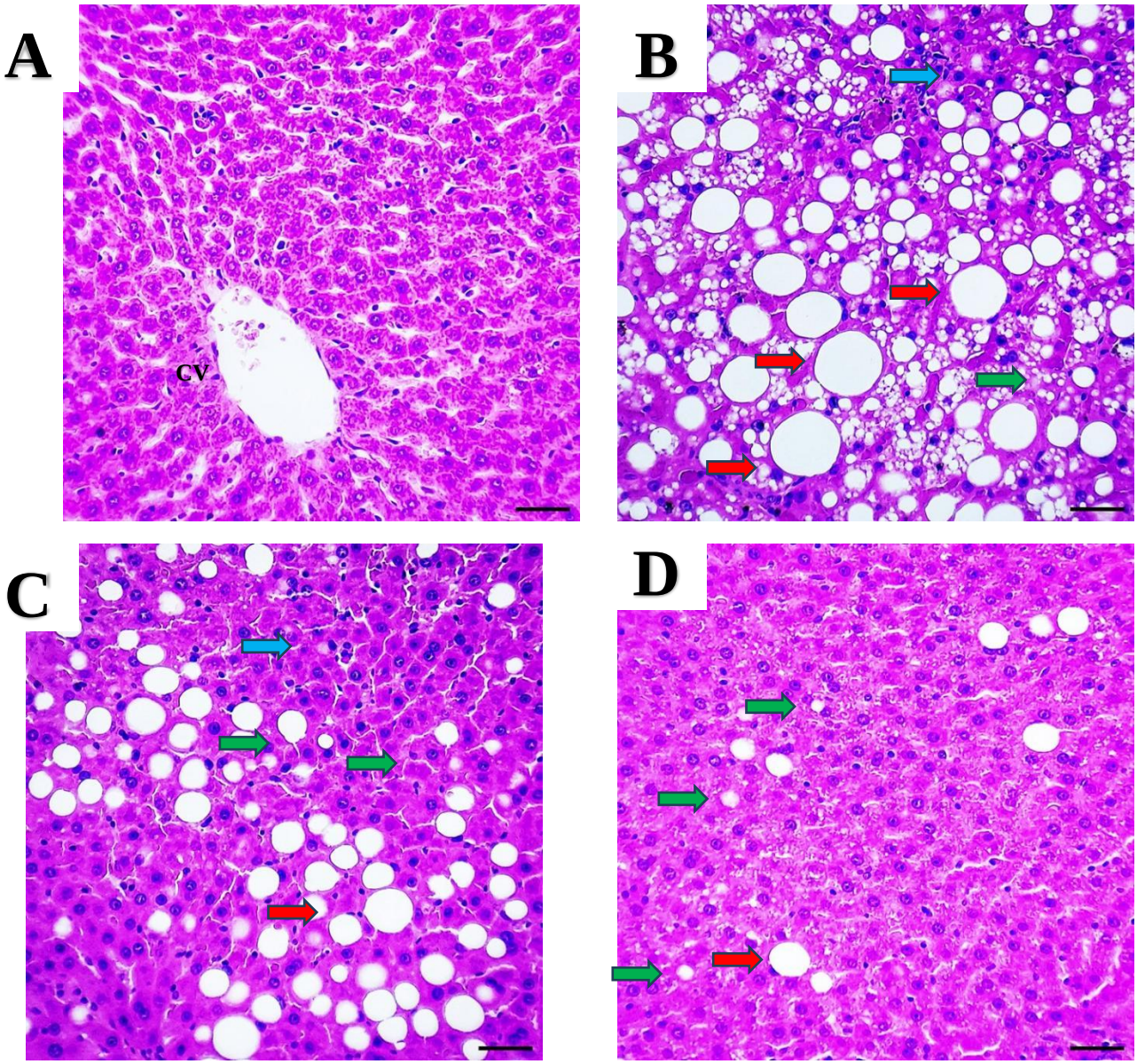

Figure Caption: Histological analysis of liver tissues across experimental groups. **Control (A)** exhibited typical liver architecture with well-organized hepatic cords, clear sinusoids, and no signs of steatosis or inflammation. **Obese, HFD-L (B)** showed significant hepatic steatosis with macro-vesicular (red arrow) as well as microvesicular (green arrow) fat accumulation, hepatocyte ballooning, pyknotic nuclei (blue arrow), and mild portal inflammation, indicative of early non-alcoholic steatohepatitis (NASH). **Obese + Orlistat (C)** demonstrated moderate improvement, with reduced lipid accumulation, decreased inflammation, and preservation of liver structure. Scale bar = 50 µm, Magnification 20x.

Table (5): Relative level of Lipid Accumulation in Liver Tissue.

Group	F 1	F 2	F 3	F 4	F 5	Average
Control (CL)	2.85	1.90	0.95	2.88	1.87	2.09
Obese (HFD-L)	24.09	30.12	20.15	29.10	14.08	23.51
Obese + ORL (Orlistat)	14.44	10.50	11.39	4.47	21.42	12.44

Conclusion:

Orlistat is a drug that used primarily for weight management by inhibiting pancreatic lipase, which reduces dietary fat absorption in the intestine. This mechanism affects not only lipid metabolism but also the body's oxidative stress levels. Inhibiting fat absorption reduces circulating triglycerides and cholesterol, which can affect a variety of metabolic pathways and oxidative stress markers, reduces fat deposition and inflammation in liver tissue.

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