Therapeutic Potential of Olive Leaf, *Plantago Ovata* Seeds, and Ginger as Anti-Obesity in Rats

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Abstract

Obesity increases cardiovascular risk, causes insulin resistance, and increases oxidative stress, leading to NAFLD and CKD. This study aims to evaluate the therapeutic potential of olive leaf, Plantago ovata seeds, and ginger in combating obesity in rats. Sixty male Wistar rats were divided into six groups: a control group (standard diet), a hyperlipidemic group (high-fat diet), and four treatment groups receiving a high-fat diet supplemented with 5% *Plantago ovata*, olive leaves, ginger, or their combination for eight weeks. Body weight and feed efficiency ratio were monitored. Blood and brain samples were analyzed to evaluate lipid profile, glucose levels, liver enzyme activity, kidney function, (oxidative stress markers and antioxidant enzymes) in the brain, were measured. The treatment groups exhibited significant weight reduction compared to the hyperlipidemic group, with the combination treatment showing the greatest effect. Additionally, the feed efficiency ratio improved in all treatment groups, particularly in the combination group. The study assessed the effects of olive leaves, psyllium, ginger, and their combination on lipid profile and glucose levels in hyperlipidemic rats. The combination group showed the greatest improvements, significantly reducing cholesterol, LDL-c, and glucose while increasing HDL-c. The tested materials and their combination improved liver and kidney function in hyperlipidemic rats, with the combination group showing the most significant reduction in AST, ALT, and creatinine levels. Olive leaves, psyllium, ginger, and their combination enhanced antioxidant enzyme activity and reduced oxidative stress in the brains of hyperlipidemic rats. The combination group exhibited the greatest decrease in MDA levels and the highest catalase, Gpx, and SOD activity. This study concluded the following: Treatment groups, especially the combination group, showed significant weight reduction, improved lipid profile, glucose levels, and liver and kidney functions. Antioxidant enzyme activity increased, while oxidative stress marker decreased, highlighting the potential of these supplements in obesity management.

Keywords: Obesity, Hyperlipidemia, *Plantago ovata*, Psyllium, Ginger, Lipids Profile, Glucose, Liver Enzymes, Kidney Functions, Antioxidant Enzymes, Oxidative Stress, Weight, Wistar Rats.

INTRODUCTION

Chronic low-grade inflammation is a persistent and systemic inflammatory response that remains below the threshold of acute inflammation but contributes to several diseases, including dyslipidemia, neurodegeneration, cardiovascular diseases, and stroke (**Visseren et al., 2021**). Dyslipidemia is an imbalance in lipid levels, characterized by high LDL cholesterol, low HDL cholesterol, and elevated triglycerides (**Byrne et al., 2022**). Patients with comorbidities, including non-communicable diseases (NCDs) and metabolic syndrome, are also at an increased risk of various cancers and chronic respiratory diseases, which collectively account for 63% of global annual deaths. Additionally, dyslipidemia is a common complication that significantly contributes to increased mortality and disease severity. It is estimated that 30%–60% of the population is affected by dyslipidemia (**Schubert et al., 2023)**. Obesity is now recognized as a major risk factor for Alzheimer’s disease (AD) due to its role in promoting chronic low-grade inflammation, insulin resistance, vascular dysfunction, and alterations in brain metabolism. The link between obesity and AD is mediated by multiple mechanisms, including neuroinflammation, lipid dysregulation, and metabolic imbalances (**Nedkoff et al., 2023)**. Alzheimer’s disease is a neurodegenerative disorder characterized by progressive neuronal loss, distinct from vascular dementia. However, major risk factors for vascular diseases—including diabetes, hypercholesterolemia, hypertension, elevated homocysteine levels, and aging—are also closely linked to the development of Alzheimer's disease (**Palacio-Portilla et al., 2022**). Elevated cholesterol levels are considered a modifiable risk factor for stroke, increasing their likelihood by 2.19 times. Additionally, high triglyceride levels contribute to a 10% rise in stroke risk. Effective regulation of dyslipidemia plays a vital role in the prevention of cardiovascular and cerebrovascular diseases (**Borén et al., 2020**). Modifying lifestyle factors, including dietary adjustments and physical activity, alongside pharmacological interventions, significantly reduces the risk of arterial and cerebral atherosclerosis **Papadaki et al., (2021)**. Various herbs and spices possess anti-inflammatory, antioxidant, and metabolic properties, making them valuable natural agents for obesity management and Alzheimer’s disease (AD) prevention. Their bioactive compounds contribute to enhancing fat metabolism, protecting neural function, and improving insulin sensitivity, all of which play crucial roles in both conditions (**Li et al., 2022**). This study aims to evaluate the therapeutic potential of olive leaf, Plantago ovata seeds, and ginger in combating obesity in rats. Specifically, it examines their effects on body weight, serum lipid profiles, glucose levels, kidney function markers, liver enzyme activities, and antioxidant defense mechanisms.

Materials and Methods

Rats:

Sixty adult male albino rats (Sprague Dawley strain), weighing 200–210 g, were obtained from the National Research Center, Dokki, Egypt. They were housed in cages under a 12:12-hour light–dark cycle (lights on from 07:00 to 19:00) at a temperature of 27 ± 2°C. The rats had free access to food and water ad libitum. All experiments were conducted accordant to standard ethical guidelines and were approved by the National Research Center Ethics Committee (7777082022).

Materials

- Casein, vitamins, minerals, cellulose, L-cystine, and choline chloride were sourced from El-Gomhoriya Company in Cairo, Egypt. Meanwhile, beef tallow, sucrose, starch, and soybean oil were procured from local markets in Cairo. Olive leaves, *Plantago ovata*, and ginger were acquired from the Agricultural Research Center in Giza, Egypt.
- **Kits and biochemical assay**: The study utilized various biochemical assay kits for analyzing lipid profile parameters, including total lipids, triglycerides, total cholesterol, and HDL-c. Additionally, oxidative stress markers such as glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) were assessed, along with lipid peroxidation indicators. Liver and kidney function markers, including alkaline phosphatase, were also evaluated. All assay kits were procured from Gama Tread Company, Cairo, Egypt.

Experimental plan and procedures

Sixty male Wistar rats were randomly assigned to six groups: *Control Group*: Received a standard diet formulated following **Reeves et al. (1993).** *Obese group*: Fed a high-fat diet based on **Min et al. (2004).** ***Treatment Groups***: Consumed a high-fat diet supplemented with 5% *Plantago ovata* (psyllium), olive leaves, or ginger. *Combination Group*: Administered a high-fat diet enriched with a 5% mixture of the tested ingredients for eight weeks. All diets were nutritionally balanced, maintaining uniform levels of vitamins, minerals, and fiber throughout the study. Body weight and feed efficiency ratio were recorded, according to **Chapman et al. (1959).** Blood samples were centrifuged at 4000 ×g for 15 minutes, with serum and plasma separated and stored at −20°C. Brain homogenates were analyzed for antioxidant enzyme activities, including superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase (CAT), expressed as units per mg of protein.

At the end of the experimental period, biochemical parameters in blood and brain tissue were analyzed as follows: The activity of antioxidant enzymes, including *superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx)*, was measured in brain tissue homogenate following the methods of **Nishikimi et al. (1972)**, **Aebi (1984)**, and **Paglia and Valentine (1967)**, respectively. Malondialdehyde (MDA), an indicator of lipid peroxidation, was assessed using the Thiobarbituric Acid Assay (TBA) according to **Draper and Hadley (1990)**. For liver function assessment, the activities of AST and ALT were determined calorimetrically following the method of **Reitman and Frankel (1957)**. Kidney function was evaluated by estimating urea levels using **Fawcett and Scott (1960)** and creatinine levels according to **Bartels et al. (1972)**. Lipid profile analysis included the measurement of triacylglycerol following **Chowdhury et al. (1971)** and total cholesterol following **Lopes-Virella et al. (1977)**. LDL and VLDL cholesterol were determined according to **Warnick et al. (1990)**. Finally, the atherogenic index was calculated as described by **Goh et al. (2004)**.

Statistical Analysis: Data were expressed as mean ± standard deviation (SD). Statistical evaluations were conducted using SPSS software (GraphPad Software Inc., San Diego, CA, USA). A one-way analysis of variance (ANOVA) was applied, followed by Duncan's multiple range test for post hoc comparisons. A P-value of ≤ 0.05 was considered statistically significant, following the methodology of **Sendecor and Cochran (1979)**.

Results and Discussion:

Obesity and hyperlipidemia are significant contributors to cerebrovascular diseases, including stroke, atherosclerosis, and compromised cerebral circulation. These conditions promote vascular inflammation, oxidative stress, and arterial plaque accumulation, ultimately impairing blood flow to the brain **(DeTure & Dickson, 2019)**. While pharmacological treatments for hyperlipidemia are widely used and effective, they are often associated with adverse effects such as muscle pain, liver dysfunction, and an increased risk of diabetes in predisposed individuals. Consequently, there is a growing interest in natural or complementary therapies that may provide lipid-lowering benefits with fewer side effects **(Byrne et al., 2023)**. Among these, *Plantago ovata* (psyllium) husk**,** olive leaf, and ginger, either individually or in combination, have gained attention for their distinct lipid-modulating properties and potential synergistic effects.

Table (1) presents the nutritional parameters of the experimental groups. The findings on body weight indicate that incorporating psyllium husk, olive leaf, ginger, or their combination into the diet helped counteract obesity. The table highlights the impact of different treatments on body weight and feed efficiency ratio in hyperlipidemic rats. Initial body weights were comparable across all groups, ensuring uniformity at the study's outset. However, the hyperlipidemic group exhibited significantly higher ($P \leq 0.05$) final body weight than the negative control group, confirming the weight-gaining effect of a high-fat diet. In contrast, all treatment groups experienced a significant ($P \leq 0.05$) reduction in final body weight compared to the hyperlipidemic group. The greatest reduction was observed in the combination group, followed by the psyllium, olive leaf, and ginger groups, demonstrating their potential effectiveness in weight management.

In terms of the feed efficiency ratio (FER), all treated groups demonstrated significantly higher values compared to the hyperlipidemic group, with the combination group exhibiting the greatest efficiency. This suggests enhanced metabolic utilization of energy. While the olive leaf group did not show a substantial reduction in final body weight like the other treatments, its relatively high FER indicates a potential role in maintaining nutritional balance without inducing significant weight loss.

Table 1: Effect of Olive Leaves, Plantago, Ginger, and Their Combination on Weight Gain and Feed Efficiency Ratio in Obese Rats

Parameter	Control Negative Group	HLD Group	(Treatment Groups)			
			Olive leafs	*Plantago ovata* (Psyllium)	Ginger	Mix
Initial body weight (gm)	200.60±2.6[a]	200.80±1.8[a]	209.40±4.1[a]	205.80±3.4[a]	203.60±3.8[a]	200.60±4.4[a]
Final body weight(gm)	342.60±8.38 [b]	443.8 ±8.2[a]	233.60±3.9[c]	228±1.7[d]	236±3[c]	216.60±3.7[e]
Feed efficiency ratio	0.59±0.048[b]	0.528 ±0.52[d]	0.595± 0.04[b]	0.662± 0.05[a]	0.684±0.03[a]	0.70±0.04[a]

HLD: Hyperlipidemic

All parameters are represented as a means of replicates ± standard Dev.

Means with different small superscript letters in the same row are significantly different at $p \leq .05$.

The findings on the feed efficiency ratio (FER) suggest that higher values indicate more effective utilization of consumed food for metabolic processes rather than being wasted. Natural compounds such as olive leaves, Plantago ovata (psyllium), ginger, and their combination have been shown to enhance metabolism, increasing energy expenditure even without changes in food intake. These treatments promote fat oxidation, facilitating the breakdown of fat stores rather than compromising food efficiency. Additionally, improved insulin sensitivity enhances nutrient uptake while supporting fat reduction. **(Gibb *et al.*, 2023)** The combination treatment demonstrated the highest FER, aligning with weight loss in obese rats, suggesting its role in preserving muscle mass while effectively reducing fat. Furthermore, enhanced digestion efficiency contributes to better nutrient absorption. Notably, no significant differences were observed in FER among the Plantago, ginger, and combination groups, indicating their effectiveness in fat reduction while maintaining metabolic balance.

A diet supplemented with olive leaves, psyllium, ginger, or their combination resulted in notable improvements in lipid fractions, as shown in Table (2). The findings reveal a strong correlation between elevated lipid profiles particularly LDL-c and triglycerides—and increased malondialdehyde (MDA) levels in the hyperlipidemic group. This underscores the role of oxidative stress in hyperlipidemia, where lipid peroxidation byproducts like

MDA not only serve as markers of oxidative damage but also contribute to atherosclerosis development. Additionally, the observed reduction in HDL-c levels may further exacerbate oxidative stress by weakening antioxidant defense mechanisms. These results collectively highlight the interconnected nature of dyslipidemia and oxidative stress in cardiovascular disease progression (**Borén et al., 2020)**. Notably, all treatment groups exhibited a significant reduction in cholesterol, triacylglycerol, and LDL-cholesterol levels compared to the hyperlipidemic group, with the most pronounced effect observed in the combination treatment group (202.21±6.0; 111.72±13.2; 75.87±7.64, respectively).

Significant variations in HDL-cholesterol levels were observed across all treatment groups, with the highest value recorded in the combination group (104.00±6.01mg/dl). Psyllium, a soluble dietary fiber extracted from *Plantago ovata* seeds, demonstrated a notable ability to lower total cholesterol and LDL-c levels. This effect is attributed to its capacity to bind bile acids, facilitating their excretion and consequently reducing circulating cholesterol levels, which reached (238.26±7.03 mg/dl). These findings align with previous research by **Nurmohamed et al. (2021)** and **Jovanovski et al. (2020).**

Olive leaves, abundant in bioactive compounds such as oleuropein and hydroxytyrosol, exhibit antioxidant, anti-inflammatory, and lipid-lowering properties, contributing to improved lipid metabolism and atherosclerosis prevention, consistent with findings by **Opara et al. (2014).** Similarly, research by **Ndezo Bisso et al. (2022)** supports the lipid-modulating effects of ginger, which contains active constituents like gingerols and shogaols. Ginger has been shown to reduce LDL-c and triglyceride levels while enhancing HDL-c, potentially through its influence on hepatic enzymes and its ability to mitigate oxidative stress, as reported by **Seo et al. (2021).**

There were improvements with significant changes between treatment groups for atherogenic index (A.I.P.). The priority of mixture group among other treatments had precious and numerous health impacts such as hypolipidemic effect due to containing of bioactive compounds that help regulate inflammation by targeting pro-inflammatory cytokines like IL-6 and oxidative stress. Our findings align with those of **Zhou (2022)**, who highlight that obesity is characterized by the expansion of adipose tissue cells, leading to heightened activity of M1 macrophages and CD8 T cells. This process is associated with an upregulation of IFN-γ, contributing to a pro-inflammatory state.

As demonstrated in Table (2) and supported by **Dowidar et al. (2019)**, olive leaf (Olea europaea), Plantago ovata (psyllium husk), and ginger (Zingiber officinale) exhibit anti-inflammatory properties by suppressing pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1β, rather than inducing their production. Additionally, an elevated atherogenic index of plasma (AIP) is associated with an increased risk of atherosclerosis, further linking obesity, hyperlipidemia, and cerebrovascular diseases.

The highest A.I.P. value was recorded in the hyperlipidemic group (0.75±0.02). As shown in Table (2), obesity contributes to elevated A.I.P. levels due to increased triglycerides from excess fat accumulation, reduced HDL-C, and heightened cardiovascular risk. Additionally, obesity often leads to metabolic syndrome, characterized by dyslipidemia and insulin resistance, which further exacerbates cerebrovascular diseases such as stroke and vascular dementia. A.I.P. plays a crucial role in promoting atherosclerosis in cerebral arteries, increasing thrombosis risk, and reducing oxygen supply to the brain, ultimately leading to ischemic stroke. Prolonged obesity also induces chronic inflammation and oxidative stress, which damage blood vessels. Similar findings by **Godoy-Matos et al. (2021)** highlight that obesity triggers neuroinflammation, as adipose tissue functions as an endocrine organ, releasing pro-inflammatory cytokines (TNF-α, IL-6, IL-1β). These cytokines penetrate the blood-brain barrier, contributing to chronic neuroinflammation. Additionally, the activation of microglia-the brain's immune cells-in response to inflammation accelerates neurodegeneration and promotes amyloid-beta plaque accumulation. Furthermore, obesity-induced gut microbiota dysbiosis increases intestinal permeability, allowing lipopolysaccharides to enter circulation, thereby aggravating brain inflammation and accelerating Alzheimer's disease progression.

This study supports the findings of **Xie et al. (2020)**, who established that obesity is strongly associated with hypertension, atherosclerosis, and diminished cerebral blood flow. These vascular impairments contribute to brain atrophy, thereby increasing the likelihood of vascular dementia and Alzheimer's disease. Moreover, hypercholesterolemia has been identified as a major risk factor, doubling the likelihood of stroke and further exacerbating cognitive decline.

The results indicate that a high-fat diet significantly increased serum glucose levels ($P \leq 0.05$) compared to the control group. Treatment with olive leaves, psyllium, ginger, and their mixture reduced glucose levels significantly ($P \leq 0.05$), with ginger and psyllium showing the most effective reduction, bringing values close to normal. The mixture, however, was less effective than some individual treatments, suggesting possible interactions. Overall, these findings highlight the potential of natural treatments in managing blood glucose levels. In this respect, **Vasarri et al. (2024)** highlighted that olive leaves are rich in bioactive compounds, particularly oleuropein, which exhibits potent anti-glycation properties. These compounds may help mitigate the formation of advanced glycation end products (AGEs), key contributors to diabetic complications. In vitro studies further support the ability of olive leaf extracts to inhibit AGE formation, suggesting a protective role against oxidative stress and inflammation in diabetes. **Gholami et al. (2024)** reported that psyllium, a soluble fiber, plays a significant role in regulating serum glucose levels, particularly in individuals with metabolic syndrome and type 2 diabetes. Systematic reviews and meta-analyses have demonstrated that psyllium consumption effectively reduces fasting blood sugar (FBS), hemoglobin A1c (HbA1c), and insulin resistance, though its impact on insulin levels remains non-significant.

Rostamkhani et al. (2023) found that ginger supplementation (2000 mg/day) significantly reduced fasting blood glucose (FBG) and insulin resistance in diabetic hemodialysis patients. Similarly, **Arzati et al. (2017)** reported significant reductions in FBG and HbA1c levels in type 2 diabetes patients after 10 weeks of supplementation.

Table (2): Effect of Olive Leaves, Plantago, Ginger, and Their Combination on Lipid Profile and Serum Glucose in Obese Rats

Groups / Parameters	Control Group	HLD Group	Treatments Groups			
			Olive leafs	*Plantago ovata* (Psyllium)	Ginger	Mixture
CHO mg/dl	114.87 ±7.5 [f]	287.77±6.9[a]	232.7±6.0 [c]	238.26±7.03 [c]	245.45±7.3[b]	202.2±6.0 [d]
HDL-c mg/dl	71.72 ±2.3 [e]	33.53 ±2.1 [f]	78.6±6.0 [d]	83.3±0.92 [c]	99.2±6.83 [b]	104.0±6.0 [a]
T.G mg/dl	78.01±8.0 [e]	190.76±7.8[a]	131.9±7.6[b]	103.6±6.52 [d]	135.4±4.6 [b]	111.7±13.2 [c]
LDL-c mg/dl	27.54 ±2.7 [e]	216.10±6.2[a]	127.7±13.2[c]	134.2± 4.63 [b]	119.2±20.3[c]	75.8±7.6 [d]
VLDL mg/dl	15.60 ±0.5 [e]	38.14±1.2[a]	26.3±1.53[b]	20.7± 1.4 [d]	27.0±3.0 [b]	22.3±1.5 [c]
A.I.P.	0.03 ±0.01 [e]	0.75±0.02[a]	0.22±0.05[b]	0.09±0.04[d]	0.13±0.02 [c]	0.03±0.0 [e]
Glucose mg/dl	89.076 ±3.5[d]	134.02±3.2[a]	100.6±1.90[c]	93.2 ±4.90 [cd]	90.14±4.4[d]	117.4±2.2 [b]

HLD: Hyperlipidemic CHO: Cholesterol HDL-c: High density lipoprotein-cholesterol

LDL-c : Low density lipoprotein-cholesterol VLDL-c : Very low density lipoprotein-cholesterol T.G. : Triglycerides A.I.P: Atherogenic index of plasma

All parameters are represented as a means of replicates ± standard Dev.

Means with different small superscript letters in the same row are significantly different at $p \leq .05$.

Liver and kidney function parameters are presented in Table 3. In the hyperlipidemic group, AST (104.08 ± 2.66 U/L) and ALT (93.48 ± 1.65 U/L) levels were significantly higher than those in the control group (AST: 46.28 ± 2.32 U/L, ALT: 33.64 ± 1.62 U/L), suggesting liver impairment associated with hyperlipidemia. Treatment with olive leaf, psyllium, ginger, and their combination significantly lowered AST and ALT levels, indicating hepatoprotective properties. The most pronounced reductions were observed in the ginger and combination groups, likely due to synergistic effects.

Creatinine and urea levels were measured to evaluate kidney function. The hyperlipidemic group exhibited significantly higher creatinine (1.09 ± 3.64 mg/dL) and urea (57.50 ± 1.59 mg/dL) levels compared to the control group (creatinine: 0.70 ± 1.56 mg/dL, urea: 46.04 ± 3.72 mg/dL), suggesting renal stress. The treatment groups significantly reduced creatinine levels, with olive leaf, psyllium, and the combination group restoring levels close to the control (~0.67 mg/dL). A similar pattern was observed in urea levels, with the combination treatment showing the greatest improvement (51.80 ± 0.63 mg/dL). ALP, an indicator of liver and bone function, was significantly elevated in the hyperlipidemic group (136.24 ± 0.09 IU/L) compared to the control group (97.16 ± 0.03 IU/L). The treatment groups exhibited a significant reduction in ALP levels, with psyllium (93.48 ± 1.91 IU/L) and the mixture group (96.17 ± 0.72 IU/L) showing the greatest improvement. This decrease suggests a potential role of these treatments in alleviating liver stress associated with hyperlipidemia. The findings of this study indicate that hyperlipidemia leads to notable disruptions in liver and kidney function, as reflected by elevated AST, ALT, creatinine, urea, and ALP levels. However, supplementation with olive leaf, psyllium, and ginger, particularly in combination, effectively counteracted these alterations, demonstrating strong hepatoprotective and renoprotective effects. The hepatoprotective effects observed in this study are consistent with previous research, including findings by **Romero-Márquez et al. (2024)**, which highlight the abundance of polyphenols in olive leaf extracts and their potent antioxidant and anti-inflammatory properties. Additionally, psyllium, a well-established dietary fiber, has been linked to enhanced lipid metabolism and may have played a role in lowering liver enzyme levels **(Abdullah et al., 2023; Gibb et al., 2023)**.

Ginger contains bioactive compounds like gingerol and shogaol, which have been shown to exhibit anti-inflammatory and lipid-lowering properties. These effects may contribute to its protective role in maintaining hepatic and renal function **(Nam et al., 2020).** The combination treatment demonstrated the greatest improvements in all biochemical parameters, indicating a synergistic interaction among these natural compounds. These results highlight the potential of these herbal treatments as complementary approaches for managing hyperlipidemia-induced liver and kidney dysfunction. Metabolic disorders, often linked to obesity and chronic inflammation, significantly affect liver and kidney function. This study underscores the impact of inflammatory markers, lipid accumulation, and oxidative stress on hepatic and renal dysfunction, reinforcing existing research on metabolic syndrome and organ damage while emphasizing the importance of early intervention (**Li et al., 2022**). The increased ALT, AST, and ALP levels in the hyperlipidemic group indicate significant hepatic stress, aligning with prior research on NAFLD and metabolic liver disorders. Liver damage associated with hyperlipidemia is primarily driven by oxidative stress due to excessive lipid accumulation in hepatocytes. This lipid overload enhances the generation of reactive oxygen species (ROS), leading to lipid peroxidation, mitochondrial dysfunction, and cellular apoptosis (**Gambini & Stromsnes, 2022**). The elevated creatinine and urea levels suggest impaired kidney function, potentially resulting from increased glomerular pressure and inflammation-induced fibrosis. These findings support the hypothesis that chronic low-grade inflammation plays a key role in multi-organ dysfunction associated with obesity. The results highlight the importance of addressing obesity-related inflammation to prevent liver and kidney damage. Alkaline phosphatase (ALP) is an enzyme primarily present in the liver, bones, kidneys, and vascular system, serving as a marker of hepatic and bone health (**Hall et al., 2021**). Although ALP is primarily linked to liver and bone disorders, recent research suggests its involvement in obesity, chronic inflammation, and cerebrovascular diseases (**El-Eshmawy et al., 2023**). Elevated ALP levels in obese individuals may be attributed to multiple factors. Obesity increases the risk of NAFLD, often leading to elevated ALP due to liver damage. Additionally, obesity influences bone turnover, potentially enhancing ALP production from osteoblasts. Furthermore, obesity-related inflammation, mediated by IL-6 and TNF-α, may stimulate hepatic ALP release (**Kim et al., 2024**).

Table (3): Effect of Olive Leaves, Plantago, Ginger, and Their Combination on Liver and Kidney Functions in Obese Rats

Parameters / Groups	Control Group	HLD Group	Treatments Groups			
			Olive leafs	*Plantago ovata* (Psyllium)	Ginger	Mix
AST U/L	46.2±2.3 [d]	104.0 ±2.6 [a]	74.28 ±2.65 [b]	56.4±4.47 [c]	48.2±2.8 [d]	46.6±1.0[d]
ALT U/L	33.6±1.6 [e]	93.4±1.6[a]	64.28 ±2.41 [b]	58.01±3.23 [c]	45.5±3.8 [d]	45.4±1.4 [d]
Creatinine mg/dl	0.7±1.5 [d]	1.09±3.6[a]	0.82 ±0.01 [b]	0.68 ±0.05 [d]	0.67 ±0.0 [d]	0.6±0.07 [d]
Urea mg/dl	46.0±3.7 [d]	57.5±1.59 [a]	52.20±1.80 [c]	55.56 ±2.23 [ab]	53.2±1.8 [b]	51.8±0.03 [c]
ALP IU/L	97.1±0. [c]	136.24 ±0.09 [a]	117.78±3.86 [b]	93.48±1.91 [c]	115.0±4.6[b]	96.1±0.72 [c]

HLD: Hyperlipidemic **AST:** Aspartate Aminotransferase **ALT:** Alanine Aminotransferase
ALP: Alkaline Phosphatase
All parameters are represented as a means of replicates ± standard Dev.
Means with different small superscript letters in the same row are significantly different at $p \leq .05$.

Malondialdehyde (MDA) is a crucial indicator of lipid peroxidation and oxidative stress. In the hyperlipidemic group, MDA levels in the brain tissues was significantly elevated (1.63±0.12 nmol/ml) compared to the control group (0.73±0.03 nmol/ml), reflecting heightened oxidative damage. Treatment with olive leaves, psyllium, ginger, and their combination significantly reduced MDA levels in the brain tissues, with the combination group showing the greatest reduction (0.91±0.05 nmol/ml). This suggests a potent antioxidant effect, likely resulting from the synergistic activity of bioactive compounds in these natural therapies. The oxidative stress induced by hyperlipidemia was further demonstrated by a significant reduction in the activity of key antioxidant enzymes, including catalase, glutathione peroxidase (GPx), and superoxide dismutase (SOD). The hyperlipidemic group exhibited a significant reduction in catalase activity (21.45±1.82 U/ml) compared to the control group (53.09±2.35 U/ml), indicating compromised antioxidant defense. Treatment with olive leaves (34.64±0.73 U/ml) and psyllium (31.73±0.86 U/ml) partially restored catalase activity, while ginger (42.81±1.41 U/ml) and the combination treatment (43.29±2.10 U/ml) demonstrated more substantial improvements. Glutathione peroxidase (GPx) activity was notably reduced in the hyperlipidemic group (21.71±0.95 U/ml). Treatment interventions effectively enhanced GPx levels, with the combination therapy (43.71±0.61 U/ml) exhibiting the most substantial improvement. Similarly, superoxide dismutase (SOD) activity was significantly diminished in the hyperlipidemic group (6.02±1.41 U/ml), indicating increased superoxide radical accumulation and heightened oxidative stress. Treatment interventions significantly restored superoxide dismutase (SOD) activity, with ginger (18.53±0.95 U/ml) and the combination therapy (19.16±0.72 U/ml) demonstrating near-normalization. These results highlight the potent antioxidant properties of olive leaves, psyllium, and ginger in counteracting oxidative stress, with the combined treatment exhibiting the greatest efficacy. The study confirms that hyperlipidemia induces marked oxidative stress, as indicated by elevated malondialdehyde (MDA) levels and reduced antioxidant enzyme activity. Supplementation with these natural antioxidants effectively enhances oxidative balance, with the synergistic effects of the combined treatment offering the most pronounced benefits. Hyperlipidemia is closely linked to oxidative stress, inflammation, and metabolic imbalances, all of which play a critical role in the development of cardiovascular and cerebrovascular diseases (**Gambini & Stromsnes, 2022**). This study assessed the effects of natural treatments, including olive leaves, psyllium, ginger, and their combination, on oxidative stress markers in hyperlipidemic rats. Findings indicate that phytochemicals in olive leaves possess anti-acetylcholinesterase and anti-cyclooxygenase-2 properties, along with strong antioxidant activity, suggesting potential neuroprotective benefits (**Yu-Jie *et al* ., 2015**). Another study emphasized that ginger exhibits antioxidant, anti-inflammatory, and neuroprotective properties, which may play a role in promoting healthy aging and preserving cognitive function **(Lockyer *et al* ., 2019**)

The findings showed a marked increase in malondialdehyde (MDA) levels in the hyperlipidemic group compared to the control, indicating heightened lipid peroxidation resulting from excessive lipid accumulation and oxidative damage. This observation is consistent with previous studies demonstrating that hyperlipidemia enhances reactive oxygen species (ROS) production, contributing to oxidative stress and cellular dysfunction (**Yang et al., 2008**).

Table (4): Effect of Olive Leaves, Plantago, Ginger, and Their Combination on Oxidative Stress and Antioxidant Enzymes in Brain Tissues of Obese Rats

Groups / Parameters	Control Group	HLD Group	Treatments Groups			
			Olive leafs	Psyllium	Ginger	Mixture
MDA (nmol/ml)	0.73±0.03 [d]	1.63±0.12 [a]	1.20±0.1 [b]	0.96±0.03 [c]	0.94±0.0 [c]	0.91±0.0[c]
Catalase U/ml	53.09±2.35 [a]	21.45±1.82 [e]	34.64±0.7 [c]	31.7±0.86[d]	42.8±1.4 [b]	43.2±2.1[b]
Gpx U/ml	50.19±3.45 [a]	21.71±0.95 [e]	33.35±1.4[d]	39.4±0.95 [c]	40.8±1.1[c]	43.7±0.6 [b]
SOD U/ml	19.19±0.25 [a]	6.02±1.41 [e]	13.94±1.6 [d]	17.3±1.0 [bc]	18.5±0.9 [ac]	19.1±0.7[a]

HLD: Hyperlipidemic **MDA:** Malondialdehyde **Gpx:** Glutathione Peroxidase **SOD:** Superoxide Dismutase
All parameters are represented as mean of replicates ± standard Dev.
Means with different small superscript letters in the same row are significantly different at $p \leq .05$.

Treatment with olive leaves, psyllium, and ginger significantly lowered MDA levels, with the combination treatment exhibiting the strongest effect. This reduction is likely due to the presence of antioxidant polyphenols and flavonoids in these natural compounds, which effectively neutralize free radicals and inhibit lipid peroxidation. Antioxidant enzyme activity was significantly compromised in the hyperlipidemic group, as evidenced by reduced levels of catalase, glutathione peroxidase (GPx), and superoxide dismutase (SOD). These enzymes are essential for neutralizing reactive oxygen species (ROS), and their decline suggests a weakened antioxidant defense system. Treatment with olive leaves, psyllium, and ginger effectively restored antioxidant enzyme activity, with the combination therapy demonstrating the greatest improvement. This enhancement may be attributed to bioactive compounds such as oleuropein in olive leaves, flavonoids in psyllium, and gingerol in ginger, which support endogenous antioxidant defense mechanisms **(Yun-chan *et al* ., 2019**). Ginger and the combination treatment exhibited the most pronounced effects, outperforming individual treatments. This suggests a possible synergistic interaction among plant-based antioxidants, enhancing their bioavailability and overall efficacy in mitigating oxidative stress. These results align with previous studies indicate that polyphenol-rich diets contribute to improved lipid metabolism and a reduction in oxidative stress under hyperlipidemic conditions.

Conclusion:

This study underscores the protective effects of olive leaves, psyllium, and ginger in reducing oxidative stress associated with hyperlipidemia, reinforcing their potential as natural therapeutic agents for managing hyperlipidemia and related metabolic disorders. Future research should investigate the molecular mechanisms underlying their antioxidant properties and evaluate their long-term impact on cardiovascular health.

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الملخص العربي

الفعالية العلاجية لأوراق الزيتون وبذور القاطونة والزنجبيل كمضادات للسمنة في الفئران

تزيد السمنة من خطر الإصابة بأمراض القلب والأوعية الدموية، وتسبب مقاومة الإنسولين، وتزيد من الإجهاد التأكسدي، مما يؤدي إلى الإصابة بمرض الكبد الدهني الغير كحولي (NAFLD) وأمراض الكلى المزمنة (CKD). تهدف هذه الدراسة إلى تقييم التاثير العلاجي لأوراق الزيتون، وبذور القطونه (Plantago ovata)، والزنجبيل في مقاومة السمنة لدى الفئران. حيث تم تقسيم ستين فأرًا من نوع ويستر (Wistar) إلى ست مجموعات: مجموعة ضابطة سالبة تتغذي علي (نظام غذائي قياسي)، مجموعة ضابطة موجبة مصابة بفرط الدهون تتغذي علي (نظام غذائي عالي الدهون)، وأربع مجموعات معاملات تتغذى على نظام عالي الدهون مضاف إليها ٥٪ من بذور القطونه، أو أوراق الزيتون، أو الزنجبيل، أو مزيج من الثلاثة لمدة ثمانية أسابيع. تمت متابعة وزن الجسم ونسبة كفاءة التغذية، وتم تحليل عينات الدم والدماغ لتقييم مستوى الدهون في الدم، مستوى الجلوكوز، نشاط إنزيمات الكبد، وظائف الكلى، مؤشرات الإجهاد التأكسدي والإنزيمات المضادة للأكسدة في الدماغ. وأظهرت مجموعات المعاملات انخفاضًا ملحوظًا في الوزن مقارنة بمجموعة فرط الدهون، وكان التأثير الأكبر لمجموعة المزيج. كما تحسنت كفاءة التغذية في جميع مجموعات المعاملات، خاصة في مجموعة المزيج. قيّمت الدراسة تأثير أوراق الزيتون، بذور القطونه، الزنجبيل، ومزيجهم على مستويات الدهون والجلوكوز في الفئران المصابة بفرط الدهون. أظهرت مجموعة المزيج أفضل النتائج، حيث خفّضت مستوي الكوليسترول، والـ LDL-c، والجلوكوز بشكل كبير، ورفعت مستوى الـ HDL-c. كما ساهمت المعاملات المستخدمة ومزيجها في تحسين وظائف الكبد والكلى، حيث أظهرت مجموعة المزيج أكبر انخفاض في مستويات إنزيمات AST وALT والكرياتينين. بالإضافة إلى ذلك، حسّنت أوراق الزيتون، وبذور القطونه، والزنجبيل ومزيجهم نشاط الإنزيمات المضادة للأكسدة، وقلّلت من الإجهاد التأكسدي بأدمغة الفئران المصابة بفرط الدهون. وأظهرت مجموعة المزيج أكبر انخفاض في مستويات MDA وأعلى نشاط لإنزيمات الكاتالاز (Catalase)، والجلوتاثيون بيروكسيداز (Gpx)، والسوبر أوكسيد ديسميوتاز (SOD). وخلصت الدراسة إلى أن مجموعات المعاملات، وخاصة مجموعة المزيج، أظهرت انخفاضًا كبيرًا في الوزن، وتحسنًا في نسب الدهون، ومستويات الجلوكوز، ووظائف الكبد والكلى، مع زيادة في نشاط الإنزيمات المضادة للأكسدة وانخفاض في مؤشرات الإجهاد التأكسدي، مما يبرز الإمكانيات الواعدة لهذه المعاملات في علاج السمنة.

الكلمات المفتاحية: السمنة، ارتفاع نسبة الدهون في الدم، لسان الحمل، الزنجبيل، الدهون، الجلوكوز، إنزيمات الكبد، وظائف الكلى، إنزيمات مضادات الأكسدة، الإجهاد التأكسدي، الوزن،