

Synergistic Anti-Inflammatory and Antioxidant Effects of Olive Leaf, *Plantago ovata*, and Ginger on Liver Histopathology in High-Fat Diet-Induced Obese Rats.

Ashraf Abd El- Aziz Abd El-Megeid¹; Sonia Saleh El-Marasy¹; Amira hamdy Abd El Aziz² and Eman F. EL-Haggar³.

1-Nutrition and Food Science Dept., Faculty of Home Economics, Helwan University.

2- Graduate student, Nutrition and food science Dept, Faculty of Home Economics , Helwan University, Egypt.

3- Nutrition and Food Science, Nutrition and Food Science Dept., Faculty of Home Economics, Arish University.

Abstract

Obesity is linked to chronic inflammation and oxidative stress, leading to metabolic disorders and liver damage. This study examined the anti-inflammatory and antioxidant effects of olive leaves, *Plantago ovata*, and ginger, individually and in combination, in an obesity-induced rat model. Sixty male Wistar rats were assigned to six groups: control (standard diet), hyperlipidemic (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 recorded. Blood and liver samples were analyzed for antioxidant enzymes (SOD, GSH-Px, CAT), while the inflammatory markers (IL-6, leptin) were determined using ELISA. Histopathological liver examinations assessed structural changes. The treatment groups showed significant reductions in final body weight compared to the hyperlipidemic group, with the combination treatment having the most pronounced effect. Feed efficiency ratio improved across all treatment groups, especially in the combination group. IL-6 and leptin levels were significantly lower, with ginger and the combination treatment exhibiting the strongest anti-inflammatory effects. Antioxidant enzyme activities (catalase, GPx, and SOD) were enhanced in all treatment groups, with the combination treatment showing the greatest improvement, indicating strong antioxidant potential. Histopathological analysis confirmed hyperlipidemia-

induced liver damage, while plant-based treatments provided varying degrees of hepatoprotection. Olive leaves, *Plantago ovata*, and ginger reduced steatosis and inflammation, with the combination treatment offering the highest protective effects. These findings suggest that combining these plant-based treatments exerts a synergistic effect, improving metabolic and inflammatory disturbances in obesity. Further research is needed to explore their potential as natural therapeutic agents for obesity-related complications.

Keywords: Obesity, Chronic Inflammation, Oxidative Stress, Antioxidant Enzymes, Olive Leaves, *Plantago ovata*, Ginger, High-Fat Diet, Histopathology.

INTRODUCTION

Obesity is a major public health issue in Egypt. A study analyzing data from a national screening of 50 million Egyptians found that Egypt ranks fourth worldwide in overall obesity rates and has the highest prevalence of female obesity, with an age-standardized rate exceeding 50% among adult women. Factors such as age, economic status, and place of residence were significantly associated with increased obesity rates. Another study estimated that obesity-related healthcare expenses in Egypt amount to approximately 62 billion EGP per year (**Esmat *et al.*, 2024**).

Obesity leads to multiple health issues, such as heart disease and strokes, placing additional strain on the healthcare system. The relationship between homeostasis, obesity, and inflammation is closely interconnected, creating a harmful cycle that impacts metabolic health. Inflammation is a direct consequence of disrupted homeostasis in obesity (**Bale *et al.*, 2022**). When homeostasis is disrupted, the body's systems, including metabolism and immune responses, do not function effectively, leading to issues such as obesity, chronic inflammation, and oxidative stress (**Ugalde-Muniz *et al.*, 2020**). Pro-inflammatory cytokines are a type of signaling protein released by immune cells that promote inflammation in response to infection, injury, or other stressors. Pro-inflammatory adipokines, such as leptin, TNF- α , IL-6, and other cytokines, play a key role in activating the immune system, helping the body defend against pathogens, repair tissues, and regulate immune responses. These pro-inflammatory adipokines contribute to chronic low-grade inflammation, insulin resistance, dyslipidemia, non-alcoholic fatty liver disease, and other metabolic syndrome-related disorders (**Pinatih *et al.*, 2023**). Chronic low-grade inflammation, characterized by elevated IL-6 levels, is implicated in the development of leptin resistance. Leptin, a hormone produced by adipocytes, regulates energy balance by suppressing appetite and increasing energy expenditure (**Kansra *et al.*, 2021**). However, in the context of obesity, despite high circulating leptin levels, the central nervous system's response to leptin is blunted, a phenomenon known as leptin resistance (**Dwipayana *et al.*, 2022**). IL-6-induced inflammation may interfere with leptin signaling pathways, exacerbating weight gain and metabolic dysfunction. IL-6 is a pro-inflammatory cytokine produced by immune cells such as macrophages and T cells, as well as adipose tissue and the liver. It acts as a pro-inflammatory

mediator, enhancing the immune response in the presence of injury or infection (Tanaka et al., 2014). Many herbs and spices contain bioactive compounds that help regulate inflammation by targeting pro-inflammatory cytokines such as IL-6, TNF- α , and IL-1 β , as well as oxidative stress. These natural compounds have been extensively studied for their anti-inflammatory, antioxidant, and immune-modulating effects (Al-Khayri et al., 2022). This study aims to evaluate the anti-inflammatory and antioxidant effects of olive leaf, *Plantago ovata*, and ginger, both individually and in combination, in an obesity-induced rat model.

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 $27 \pm 2^\circ\text{C}$. The rats had free access to food and water ad libitum. All experiments were conducted in accordance with standard ethical guidelines and were approved by the National Research Center Ethics Committee number (7777082022).

Materials

Casein, vitamins, minerals, cellulose, L-cystine, and choline chloride were obtained from El-Gomhoriya Company, Cairo, Egypt. Beef tallow, sucrose, starch, and soybean oil were purchased from the local market in Cairo, Egypt. Olive leaves, *Plantago ovata*, and ginger were obtained from the Agricultural Research Center, Giza, Egypt.

Kits: Inflammatory markers, including IL-6 and leptin hormone, and oxidative stress markers, including glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), and catalase (CAT), were used. All kits were obtained from Gama Tread Company, Cairo, Egypt.

Experimental plan and procedures

Sixty male Wistar rats were divided into six groups: *Control group*: Fed a standard diet prepared according to Reeves et al. (1993). *Hyperlipidemic group*: Fed a high-fat diet prepared according to Min et al. (2004). *Treatment groups*: Fed a high-fat diet supplemented with 5% “*Plantago ovata* (psyllium), olive leaves, or ginger”. *Combination group*: Fed a high-fat diet supplemented

with 5% of the mixture of these tested materials for 8 weeks. All diets maintained consistent levels of vitamins, minerals, and fiber throughout the 8-week experimental period. Body weight and feed intake were recorded weekly. Nutritional evaluation was conducted following the methodology outlined by **Chapman et al. (1959)**. Blood samples were centrifuged at $4,000 \times g$ for 15 minutes, and the separated serum and plasma were stored at -20°C . A 10% liver homogenate was prepared to determine the activities of SOD, GSH-Px, and CAT (units/mg protein). **Inflammation Markers:** IL-6, leptin measured via ELISA.

Histopathological Examination:

The rat livers were subjected to histopathological examination at the Faculty of Veterinary Medicine, Cairo University, Cairo, Egypt.

Statistical Analysis:

Data were presented as mean \pm standard deviation (SD). Statistical analysis was performed using SPSS (GraphPad Software Inc., San Diego, CA, USA). One-way analysis of variance (ANOVA) was conducted, followed by Duncan's multiple range test. The significance level of $P \leq 0.05$ was considered statistically significant (**Sendecor and Cochran 1979**).

Results and discussion:

Obesity and hyperlipidemia are major risk factors for cerebrovascular diseases such as stroke, atherosclerosis, and reduced brain circulation. These conditions contribute to vascular inflammation, oxidative stress, and plaque buildup, leading to impaired blood flow to the brain (**DeTure and Dickson, 2019**). Current treatment strategies for hyperlipidemia largely rely on pharmacological interventions, which are often effective but present adverse side effects like muscle pain, liver dysfunction, and a risk of diabetes in susceptible individuals. This has driven an increasing interest in alternative or complementary therapies derived from natural sources, offering potential benefits with fewer side effects (**Byrne et al., 2023**). Among the natural compounds investigated for their hypolipidemic properties, *Plantago ovata*

(psyllium) husk, olive leaf, ginger, and their mixture stand out for their unique mechanisms of action and synergistic potential.

Nutritional parameters of different experimental groups are illustrated in Table (1). The results of body weight for experimental animals assert that feeding a diet containing psyllium husk, olive leaf, ginger, and their mixture caused a corrective attitude to obesity. The table illustrates the effects of different treatments on body weight and feed efficiency ratio in hyperlipidemic rats. There was no significant difference in initial body weight among all groups, indicating homogeneity before the experiment. However, the final body weight was significantly higher $P \leq 0.05$ in the hyperlipidemic group compared to the control negative group, confirming the impact of a high-fat diet on weight gain. In contrast, all treatment groups showed a significant reduction $P \leq 0.05$ in final body weight compared to the hyperlipidemic group, with the most pronounced effect in the mix group, followed by the *Plantago ovata* (psyllium), olive leaves, and ginger groups, suggesting their potential role in weight reduction.

Regarding the feed efficiency ratio (FER), the treated groups showed significantly higher values compared to the hyperlipidemic group, with the mix group having the highest efficiency, indicating improved metabolic utilization of energy. Although the olive leaf group did not show a significant reduction in final weight like other treatments, its feed efficiency ratio was relatively high, suggesting a potential role in nutritional balance without drastic weight loss.

The results of the feed efficacy ratio (FER) confirm that the higher means that more of the consumed food is being used effectively for body processes rather than wasted. Certain natural resources used for weight loss, e.g., olive leaves, *Plantago ovata* (psyllium), ginger, or their mixture, can boost metabolism, leading to higher energy expenditure even with the same food intake.

Increase fat oxidation, leading to breaking down fat stores rather than reducing food efficiency. So, improving insulin sensitivity caused enhanced nutrient uptake while promoting fat loss. The mixture treatment has the highest FER. A line with weight loss in obese rats suggests that the mixture might be preserving muscle mass while burning fat effectively. Also, improve digestion by making the body process food more efficiently. There were no significant differences

between Plantago, ginger, or mixture in FER This means these treatments are working efficiently in fat reduction while maintaining metabolic health.

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

Parameter	Control Negative Group	Hyperlipidemic Group	(Treatment Groups)			
			Olive leafs	<i>Plantago ovata</i> (Psyllium)	Ginger	Mix
Initial body weight	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	342.600±8.38 ^b	443.8 ±8.2 ^a	233.60±3.9 ^c	228±1.7 ^d	236±3 ^c	216.60±3.7 ^c
Feed efficiency ratio	0.59580±0.048 ^b	0.528 ±0.52 ^d	0.595± 0.04 ^b	0.662± 0.05 ^a	0.684±0.03 ^a	0.707±0.04 ^a

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 $p \leq .05$.

Inflammation markers:

This study highlights the detrimental effects of hyperlipidemia on liver health and investigates the potential protective roles of olive leaf, *Plantago ovata*, ginger, and their combination. Hyperlipidemia is a major contributor to systemic inflammation, primarily driven by adipokines and pro-inflammatory cytokines. Leptin and IL-6 play central roles in this inflammatory cascade (Gulo et al., 2022). Olive leaf (*Olea europaea*), *Plantago ovata* (psyllium husk), and ginger (*Zingiber officinale*) do not promote pro-inflammatory cytokine production. Instead, they possess anti-inflammatory properties by suppressing cytokines such as IL-6, TNF-α, and IL-1β. Similar findings were documented by Nyangasa et al. (2020). This effect was evident in treatments with olive leaves, *Plantago ovata*, ginger, and their combination, all of which effectively reduced IL-6 and leptin levels to varying degrees. Ginger and the mixture exhibited the greatest reductions in IL-6 (↓62.79% and ↓61.26%, respectively), indicating a strong anti-inflammatory effect. Leptin levels showed the most significant decreases in the mixture (↓65.96%) and ginger

(↓62.78%) groups, suggesting their potential role in enhancing leptin sensitivity and promoting metabolic balance (Table 2). Olive leaves and *Plantago ovata* demonstrated moderate effects, suggesting individual antioxidant and anti-inflammatory properties, though less potent than the mixture. These findings indicate that combining plant-based bioactive compounds—such as olive polyphenols, gingerols, and *Plantago* flavonoids—may enhance anti-inflammatory effects, making the mixture treatment the most effective. This could have therapeutic potential in managing metabolic inflammation and hyperlipidemia. Additionally, our results revealed a significant increase in IL-6 and leptin levels in the hyperlipidemic group, aligning with the findings of **Stelzer et al. (2012)**, who established a direct link between leptin and IL-6 in the early stages of obesity-related inflammation. Leptin, a hormone secreted by adipocytes, plays a key role in immune cell activation and cytokine production, contributing to chronic inflammation in metabolic disorders.

Similarly, **Ellulu et al. (2017)** emphasized that obesity and hyperlipidemia trigger a low-grade chronic inflammatory response, exacerbating oxidative stress and contributing to insulin resistance and metabolic dysfunction. This aligns with our histological findings, where the hyperlipidemic group exhibited significant hepatocyte steatosis and mononuclear inflammatory cell infiltration, indicating an inflammatory response in liver tissue.

Our results further demonstrate that hyperlipidemia significantly increases oxidative stress and inflammation, leading to hepatocyte damage. However, natural plant extracts—olive leaf, *Plantago ovata*, and ginger—provided varying degrees of hepatoprotection. These findings are consistent with previous research, reinforcing the link between inflammation, oxidative stress, and metabolic dysfunction in hyperlipidemia (**Soomro, 2019**). Furthermore, research by **Gomez-Apo et al. (2022)** demonstrated that peripheral inflammation originating from adipose tissue and the liver can affect brain function, contributing to metabolic and neurological disorders. This suggests that hyperlipidemia-induced inflammation extends beyond the liver, disrupting whole-body homeostasis.

Table (2) Effect of Olive Leaves, Plantago, Ginger, and Their Combination on IL-6 and Leptin Levels in Treatment Groups Compared to the Hyperlipidemic Group

Parameter	Hyperlipidemic Group	% Change (Treatments VS. Control Group)			
		Olive leafs	Plantago	Ginger	Mix
IL-6 (pg/mL)	17.50 ±1.19	↓52.785	↓47.427	↓62.790	↓61.2622
Leptin (ng/mL)	34.31 ±1.34	↓28.85	↓26.40	↓62.78	↓65.96

Oxidative Stress Markers:

The results indicate that hyperlipidemia significantly reduces antioxidant enzyme activity in the liver, as observed in the hyperlipidemic group (Table 3). However, treatment with olive leaves, Plantago, ginger, and their combination effectively restored antioxidant enzyme levels, with varying degrees of improvement. Our study highlights the detrimental effects of hyperlipidemia on liver health and the potential protective role of olive leaves, Plantago, ginger, and their combination. Hyperlipidemia is a key driver of systemic inflammation, primarily mediated by adipokines and pro-inflammatory cytokines, with leptin and IL-6 playing central roles in this inflammatory cascade. These findings are consistent with previous research, further reinforcing the connection between inflammation, oxidative stress, and metabolic dysfunction in hyperlipidemia (Eldesoky et al., 2018). Oxidative stress triggers inflammation in hyperlipidemia-induced liver dysfunction. This study investigated the hepatoprotective potential of olive leaf, Plantago, ginger, and their combination. Olive leaf treatment significantly reduced hepatic damage, consistent with research on oleuropein a potent polyphenol in olive leaves known for its ability to mitigate lipid accumulation and oxidative stress

by modulating AMPK activation and inflammatory pathways (Andersen, 2022). Plantago provided moderate liver protection but was less effective than the combination treatment. Kim et al. (2024) reported that plantago-derived bioactive compounds, including polysaccharides and flavonoids, regulate inflammatory responses, which may explain its partial hepatoprotective effects. Ginger treatment effectively reduced oxidative stress and inflammation, supporting previous findings on gingerols and shogaols as potent free radical scavengers and anti-inflammatory agents. The combination treatment demonstrated the greatest improvement, suggesting a synergistic hepatoprotective effect. This is consistent with the findings of Le Thuc & García-Cáceres (2024), who highlighted that multi-component phytotherapies offer superior metabolic and anti-inflammatory benefits compared to single-compound treatments.

Table (3) Effect of Olive Leaves, Plantago, Ginger, and Their Combination on Liver Enzymes, Including Catalase, Glutathione Peroxidase, and Superoxide Dismutase, in Treatment Groups Compared to the Hyperlipidemic Group.

Groups Parameter	Control Group	Hyperlipidemic Group	Treatments Groups			
			Olive leafs	Plantago	Ginger	Mix
Catalase (Liver,U/mL)	155.1±5.23 ^a	71.29± 2.9 ^e	96.1± 1.0 ^c	94.4± 4.1 ^c	91.2± 1.3 ^b	116.2± 3.4 ^b
GPx (Liver,U/mL)	35.5±1.80 ^c	24.13± 2.4 ^f	34.1± 1.3 ^{d c}	33.0± 3.1 ^{d c}	40.8± 2.5 ^b	45.2± 1.5 ^a
SOD (Liver,U/mL)	57.0±2.07 ^b	37.26± 2.2 ^e	43.2± 3.7 ^d	52.7± 2.6 ^c	63.6± 1.8 ^a	64.7± 2.7 ^a

All parameters are represented as mean of replicates ± standard Dev.

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

The mixture treatment demonstrated the most significant improvement across all parameters, suggesting a potential synergistic effect. Among

individual treatments, ginger was the most effective in enhancing glutathione peroxidase ($\uparrow 69.1\%$) and superoxide dismutase ($\uparrow 70.8\%$) activity, highlighting its strong antioxidant properties. Olive leaves and plantago also increased antioxidant enzyme levels, though their effects were moderate compared to the mixture. Catalase levels showed the highest increase in the mixture group ($\uparrow 63.0\%$), indicating improved hydrogen peroxide detoxification and oxidative stress defense. These findings suggest that combining antioxidant-rich plants may provide superior protection against hyperlipidemia-induced oxidative stress compared to individual treatments. The mixture treatment demonstrated the highest increase ($\uparrow 63.0\%$) in catalase activity, indicating enhanced hydrogen peroxide detoxification and reduced oxidative damage.

Olive ($\uparrow 34.8\%$) and Plantago ($\uparrow 32.4\%$) exhibited moderate effects, indicating individual antioxidant capacity, though less potent than the mixture. Hyperlipidemia reduced catalase activity by approximately 54%, leading to increased oxidative stress. The observed improvements may be attributed to polyphenols from olive and Plantago (e.g., oleuropein and flavonoids), which stimulate Nrf2 activation, enhancing catalase expression. Additionally, gingerols in ginger help reduce lipid peroxidation, preserving catalase activity. The synergistic effect observed in the mixture may involve multiple pathways that enhance enzyme activity more effectively.

Histopathological Examination Results:

The histopathological examination of liver sections in this study highlights the damaging effects of hyperlipidemia and the protective potential of plant-based treatments. The control group exhibited normal hepatic architecture, confirming healthy liver structure. The liver structure is intact, with no abnormalities observed. Fig (1) shows normal liver structure with well-preserved hepatic lobules with no signs of fat accumulation, inflammation, or degeneration. In contrast, the hyperlipidemic group (Fig 2) displayed severe hepatocyte steatosis and inflammatory cell infiltration; there was mononuclear inflammatory cell infiltration commonly seen in non-alcoholic fatty liver disease (NAFLD), alcoholic liver disease, obesity, or metabolic disorders. Figure (2) indicates liver damage caused by excessive lipid accumulation and an inflammatory response. This aligns with previous research (Ellulu et al.,

2017), which confirms hyperlipidemia contributes to hepatocellular injury and chronic inflammation. The treatment groups demonstrated varying degrees of hepatoprotection. The olive and plantago groups showed moderate hepatocyte steatosis with inflammatory infiltration, indicating partial protection (Figs. 3 & 4). This finding is in line with **Eldesoky et al. (2018)**, who reported that olive-derived polyphenols and psyllium fiber may have beneficial effects in mitigating liver damage due to their lipid-lowering and anti-inflammatory properties. Additionally, the ginger-treated group exhibited vacuolar degeneration and Kupffer cell proliferation as signs of stress but with some healing effects (Fig. 5) and confirmed some hepatoprotective effects. The beneficial properties of ginger can be attributed to its bioactive compounds, including gingerol, shogaol, and zingerone, which possess antioxidant, anti-inflammatory, and hepatoprotective activities (**Jazayeri et al., 2021**). Interestingly, the mixture group manifested the best improvement, with minimal vacuolar degeneration and slight Kupffer cell activation, indicating enhanced liver protection and reduced inflammation (Fig. 6). These results suggest that the combination of plant-based treatments may exert a synergistic effect, offering a more effective strategy for preserving liver structure and function. **Kapiotis et al. (2006)** further support this notion, indicating that gingerols from ginger and oleuropein from olive leaves help modulate inflammatory markers such as IL-6 and TNF- α , thereby breaking the cycle of inflammation. Beyond hepatic health, the implications of these findings extend to cognitive function. Liver dysfunction, particularly due to hyperlipidemia, has been linked to neuro-inflammation and cognitive decline. The liver plays a crucial role in metabolizing lipids and regulating systemic inflammation; thus, hepatic dysfunction can contribute to neurodegenerative diseases through increased oxidative stress and inflammatory mediators. Given that oxidative stress and chronic inflammation are major contributors to neurodegenerative conditions such as Alzheimer's disease, the observed hepatoprotective effects of these plant-based treatments may also have potential benefits for cognitive health. Polyphenols and bioactive compounds in ginger, olive, and Plantago have been shown to exert neuroprotective effects by reducing oxidative damage, enhancing mitochondrial function, and modulating inflammatory pathways in the brain (**Jazayeri et al., 2021**).

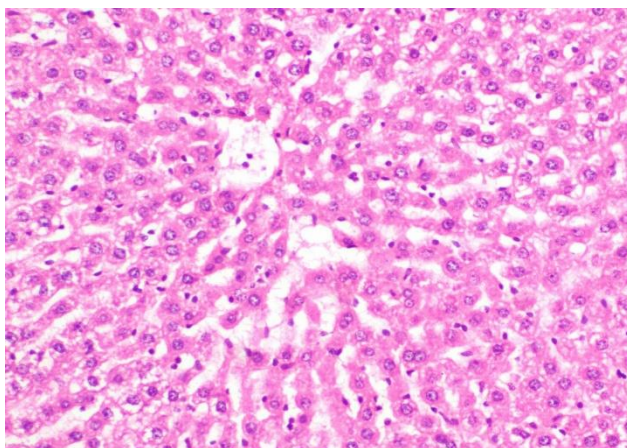


Fig. (1): The microscopic image shows a section of the liver from a rat in Group 1, which serves as the control group. The liver tissue displays a normal histological structure, meaning that the liver cells (hepatocytes) and their organization within the hepatic lobules are intact and free of abnormalities.

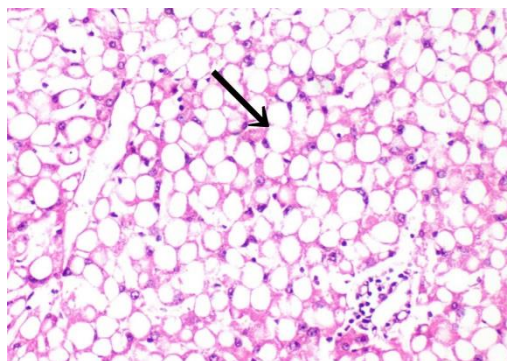
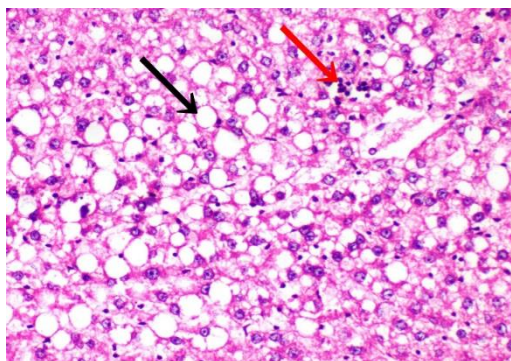


Fig. (2): The microscopic image shows a section of the liver of a rat from the hyperlipidemic group showing hepatocellular steatosis (arrow) and mononuclear inflammatory cell infiltration (red arrow).

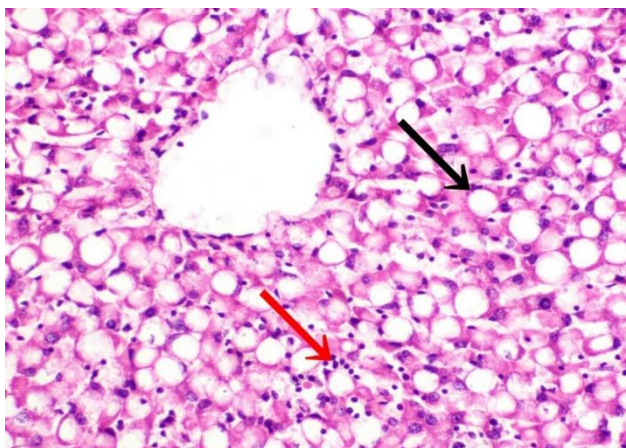


Fig. (3): The microscopic image shows a section of liver of rat from olive showing hepatocellular microvesicular steatosis of some hepatocytes (black arrow) and slight Kupffer cell proliferation (red arrow).

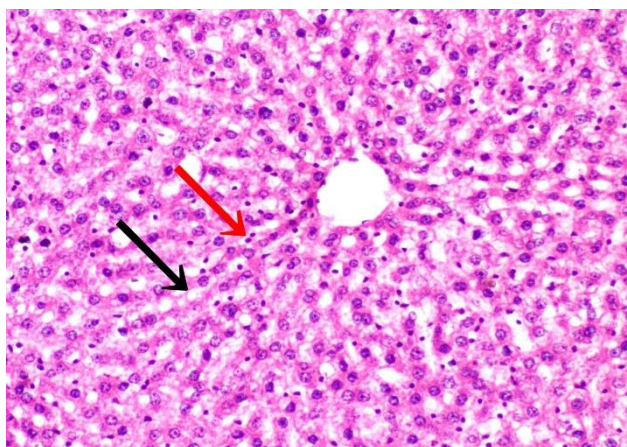


Fig. (4): The microscopic image shows a section of the liver of rat from Plantago showing hepatocellular microvesicular steatosis of some hepatocytes (black arrow) and slight Kupffer cell proliferation (red arrow).

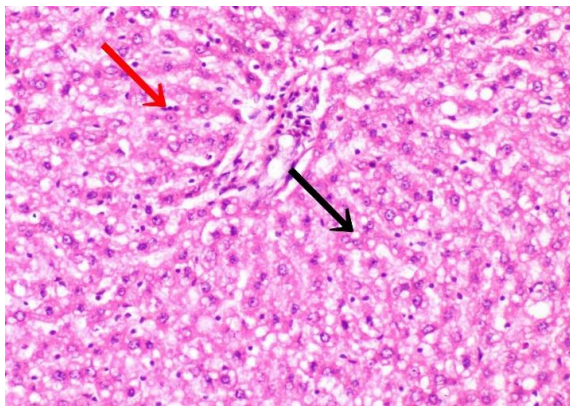


Fig. (5): The microscopic image shows a section of liver of rat from the ginger group showing hepatocellular vacuolar degeneration of hepatocytes (black arrow) and slight Kupffer cell proliferation (red arrow).

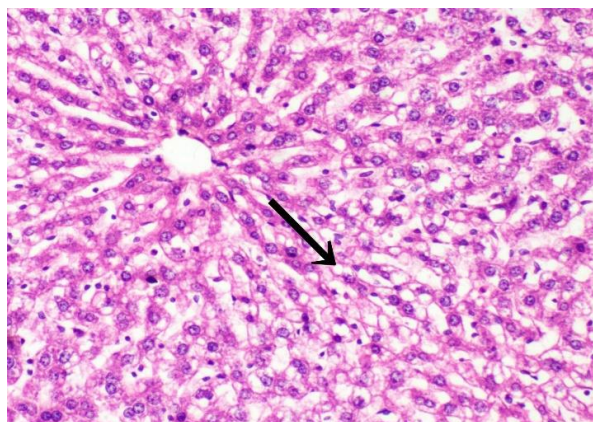


Fig. (6): The microscopic image shows a section of the liver of a rat from the mixture group showing vacuolar degeneration of some hepatocytes (black arrow).

In conclusion, hyperlipidemia-induced liver damage is associated with significant hepatocyte steatosis and inflammation, which may have systemic consequences, including cognitive impairment. The findings of this study suggest that plant-based treatments, particularly a combination of Plantago, Olive, and Ginger, offer a promising hepatoprotective strategy. Future studies should explore the long-term effects of these treatments on both hepatic and neurological health, further elucidating the link between liver function and cognitive decline.

CONCLUSION

The study reveals that hyperlipidemia significantly impairs antioxidant enzyme activity, which leading to elevated oxidative stress and contributes to liver dysfunction. Treatment with olive leafs, Plantago, ginger, and their combination effectively renew antioxidant defenses, Moreover the combination treatment exhibiting the highest enhancement among all evaluated parameters.

REFERENCES:

- Al-Khayri, J. M., Sahana, G. R., Nagella, P., Joseph, B. V., Alessa, F. M., and Al-Mssallem, M. Q. (2022).** Flavonoids as potential anti-inflammatory molecules: A review. *Molecules*, 27(9), 2901.
- Andersen, C. J. (2022).** Lipid metabolism in inflammation and immune function. *Nutrients*, 14(1414).
- Bale, B. F., Doneen, A. L., Leimgruber, P. P., & Vigerust, D. J. (2022).** The critical issue linking lipids and inflammation: Clinical utility of stopping oxidative stress. *Frontiers in Cardiovascular Medicine*, 9, 1042729.
- Byrne, R. A., Rossello, X., Coughlan, J. J., Barbato, E., Berry, C., and Chieffo, A. (2023).** ESC guidelines for the management of acute coronary syndromes. *European Heart Journal*, 44(38), 3720–3826.
- Chapman, D. G., Castilla, R., and Campbell, J. A. (1959).** Evaluation of protein in food: Method for the determination of protein efficiency ratio. *Canadian Journal of Biochemistry and Physiology*, 37, 679-686.
- DeTure, M. A., and Dickson, D. W. (2019).** The neuropathological diagnosis of Alzheimer's disease. *Molecular Neurodegeneration*, 14, 32, 2-18.
- Dwipayana, I. M. P., Gotera, W., Suastika, K., Yasa, I. W. P. S., Budhiarta, A. A. G., and Saraswati, M. R. (2022).** Association between insulin, glucagon, high-sensitive C-reactive protein, insulin resistance with visceral adipose tissue-derived serine protease inhibitor (VASPIN) in obese population. *Bali Medical Journal*, 11(3), 1717–1720.
- Eldesoky, A. H., Abdel-Rahman, R. F., and Ahmed, O. K. (2018).** Antioxidant and hepatoprotective potential of *Plantago major* growing in

Egypt and its major phenylethanoid glycoside, acteoside. *Journal of Food Biochemistry*, 42, e12567.

Ellulu, M. S., Patimah, I., Khaza'ai, H., Rahmat, A., and Abed, Y. (2017). Obesity and inflammation: The linking mechanism and the complications. *Archives of Medical Science*, 13, 851–863.

Esmat, G., Zaid, H., and Hassany, M. (2024). Obesity prevalence in adults and patients with hepatitis C: Results from screening a population of 50 million in Egypt. *Egyptian Liver Journal*, 14, 22.

Gomez-Apo, E., Mondragon-Maya, A., Ferrari-Diaz, M., and Silva-Pereyra, J. (2021). Structural brain changes associated with overweight and obesity. *Journal of Obesity*, 2021, 6613385.

Gulo, C. I. H., Puruhito, N., and Novida, H. (2022). The effectiveness of topical hyaluronic acid on decreasing interleukin-6 and acceleration of wound healing (Push Score) in Wagner II-III diabetic foot ulcer in Dr. Soetomo Hospital Surabaya. *Bali Medical Journal*, 11(3), 1049–1053.

Jazayeri, S. F., Ghods, R., Hashem Dabaghian, F., Shojaii, A., Moravej, S. A. A., Khadem, E., and Seyedian, S. S. (2021). The efficacy of *Plantago major* seed on liver enzymes in nonalcoholic fatty liver disease: A randomized double-blind clinical trial. *Evidence-Based Complementary and Alternative Medicine*, 2021, 6693887.

Kansra, A. R., Lakkunarajah, S., and Jay, M. S. (2021). Childhood and adolescent obesity: A review. *Frontiers in Pediatrics*, 8, 581461.

Kapiotis, S., Holzer, G., Schaller, G., Haumer, M., Widhalm, H., Weghuber, D. (2006). A proinflammatory state is detectable in obese children and is accompanied by functional and morphological vascular changes. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 26(11), 2541–2546.

Kim, K.H., Hwang, Y., and Kang, S-S. (2024). Regulatory Effect of Spray-Dried Lactiplantibacillus plantarum K79 on the Activation of Vasodilatory Factors and Inflammatory Responses, *Food Science of Animal Resources*, 44, 1, (216–224),

Le Thuc, O., and García-Cáceres, C. (2024). Obesity-induced inflammation: Connecting the periphery to the brain. *Nature Metabolism*, 6, 1237–1252.

- Min, L., Ling, S., Yin, L., Stephen, C. W., Randy, J. S., David, D., and Patrick, T. (2004).** Obesity induced by a high-fat diet downregulates apolipoprotein A-IV gene expression in rat hypothalamus. *American Journal of Physiology-Endocrinology and Metabolism*, 287, E366–E370.
- Nyangasa, M. A., Buck, C., Kelm, S., Sheikh, M. A., Günther, K., and Hebestreit, A. (2020).** The association between leptin and inflammatory markers with obesity indices in Zanzibari children, adolescents, and adults. *Obesity Science & Practice*, 7(1), 71–81.
- Reeves, P.G., Nielsen, F.H., and Fahey, G.C., (1993).** AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-76A rodent diet.” *J. Nutr.* 123, 1939-51.
- Sendecor, G., and Cochran, W. (1979).** *Statistical methods* (6th ed.). Iowa State College, U.S.A.
- Soomro, S. (2019).** Oxidative stress and inflammation. *Open Journal of Immunology*, 9, 1-20.
- Stelzer, I., Zelzer, S., Raggam, R. B., Prüller, F., Truschnig-Wilders, M., and Meinitzer, A., (2012).** Link between leptin and interleukin-6 levels in the initial phase of obesity-related inflammation. *Translational Research*, 159(2), 118–124.
- Tanaka, T., Narazaki, M., and Kishimoto, T. (2014).** IL-6 in inflammation, immunity, and disease. *Cold Spring Harbor Perspectives in Biology*, 6(10), a016295.
- Ugalde-Muniz, P., Fetter-Pruneda, I., Navarro, L., Garcia, E., & Chavarria, A. (2020).** Chronic systemic inflammation exacerbates neurotoxicity in a Parkinson’s disease model. *Oxidative Medicine and Cellular Longevity*, 2020, 4807179.

الملخص العربي

"الخصائص المضادة للالتهاب والأكسدة لأوراق الزيتون وبذور القاطونة والزنجبيل، ودراسة تأثيرها علي التغيرات الهستوباثولوجية في الكبد لدي الفئران المصابة بالسمنة"

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 التأثير العلاجي لأوراق الزيتون، وبذور القطونه (*Plantago ovata*)، والزنجبيل في مقاومة السمنة لدى الفئران. حيث تم تقسيم ستين فأراً من نوع ويستار (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 تتغذي علي 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 انخفاضاً ملحوظاً في الوزن مقارنة بمجموعة فرط الدهون، وكان التأثير الأكبر لمجموعة المزيج. كما تحسنت كفاءة التغذية في جميع مجموعات المعاملات، خاصة في مجموعة المزيج. قُيِّمت الدراسة تأثير أوراق الزيتون، بذور القطونه، الزنجبيل، ومزيجهم على مستويات الدهون والجلوكوز في الفئران المصابة بفرط الدهون. أظهرت مجموعة المزيج أفضل النتائج، حيث خُفِّضت مستوى 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 و ALT والكرياتينين. بالإضافة إلى ذلك، حسَّنت أوراق الزيتون، وبذور القطونه، والزنجبيل ومزيجهم نشاط الإنزيمات المضادة للأكسدة، وقلَّلت 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 المزيغ، أظهرت انخفاضًا كبيرًا في الوزن، وتحسنًا في نسب الدهون، ومستويات الجلوكوز، ووظائف الكبد والكلية، مع زيادة في نشاط الإنزيمات المضادة للأكسدة وانخفاض في مؤشرات الإجهاد التأكسدي، مما يبرز الإمكانيات الواعدة لهذه المعاملات في علاج السمنة.

الكلمات المفتاحية: السمنة، التهاب المزمن، الإجهاد التأكسدي، إنزيمات مضادات الأكسدة، أوراق الزيتون، لسان الحمل البضاوي، الزنجبيل، النظام الغذائي عالي الدهون، علم الأمراض النسيجي.