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Histopathological Assessments of Obese Rats Supplemented with *Sargassum muticum* from the Moroccan Atlantic Coast Show Reduced Obesity-Related Organ Alterations

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Abstract

Obesity is a chronic systemic disorder frequently associated with multiorgan complications of inflammatory and metabolic origin. This study aimed to evaluate the histoprotective effects of *Sargassum muticum*, an invasive brown seaweed harvested from the Moroccan Atlantic coast, in cafeteria diet-induced obese rats. Thirty-five Wistar rats were divided into five groups: standard control, obese control (cafeteria diet), two obese groups treated with *Sargassum muticum* at 10% and 20%, and one group treated with orlistat at 30 mg/kg. After eight weeks, tissue samples were collected for a histopathological analysis. In untreated obese rats, histological examination revealed multiple abnormalities, including submucosal edema, vascular congestion, gastric inflammatory infiltration, pulmonary hemorrhage and lipid vacuoles, as well as hepatic, cardiac, pancreatic, and testicular lesions. Treatment with *S. muticum*, particularly at 20%, markedly improved these alterations, characterized by a significant reduction in inflammatory infiltration, vascular congestion, lipid vacuolization, and tissue degeneration, together with improved preservation of tissue architecture. These effects were superior to those observed with orlistat. The anti-inflammatory, antioxidant, and metabolic properties of *S. muticum* are likely due to its richness in bioactive compounds, notably phlorotannins, fucoxanthin, and sulfated polysaccharides. These findings confirm the therapeutic potential of *S. muticum* in preventing histopathological complications of obesity and pave the way for translational studies and potential nutraceutical applications in human obesity management.

Keywords: *Sargassum muticum*; obesity; histopathology; brown algae; cafeteria diet; Wistar rats

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1. Introduction

Obesity is now recognized as a chronic multifactorial disease involving hormonal, metabolic, and inflammatory imbalances. It represents a major global public health challenge, affecting millions of individuals worldwide. Recent statistics indicate that 650 million people suffer from obesity, while approximately 1.9 billion are overweight [1]. This epidemic affects all age groups and has significant health, societal, and economic consequences due to the high costs and associated pathologies.

Among its most common comorbidities are cardiovascular diseases, non-alcoholic fatty liver disease (NAFLD), type 2 diabetes, kidney disorders, chronic respiratory conditions, and neurological impairments, which collectively contribute to obesity-related multiorgan dysfunction. These complications share common underlying mechanisms, notably low-grade chronic inflammation and oxidative stress [2]. Such mechanisms often lead to characteristic histopathological changes, including inflammatory cell infiltration, tissue fibrosis, and structural disruptions in vital organs.

In this context, natural products such as marine algae are drawing increasing interest due to their richness in bioactive compounds [3]. *Sargassum muticum*, an invasive brown alga introduced to the Moroccan northwestern Atlantic coast in 2011 [4], stands out not only for its nutritional profile rich in fiber, essential minerals, and vitamins [5] but also for its high content of fucoxanthin, saringosterol, phlorotannins, fucoidan, and alginates, which are known for their antioxidant, anti-inflammatory, and metabolic properties [6]. Although our study is currently under publication highlighted the effectiveness of *S. muticum* on anthropometric and biochemical parameters related to obesity, its role in modulating associated histopathological alterations remains poorly explored, particularly in the context of invasive species studied in Morocco.

This study is original in evaluating an invasive Moroccan macroalga as a potential therapeutic agent, exploring its protective or restorative effects on obesity-induced tissue damage. Beyond its pharmacological interest, this approach also has important ecological and socio-economic implications, as *S. muticum* has caused significant disturbances to coastal ecosystems along the Moroccan Atlantic coast [4]. Its valorization as a therapeutic and nutraceutical resource may contribute to mitigating the ecological impact of its invasion while creating added economic value, with potential relevance for other regions affected by the spread of this species.

This study thus aims to evaluate the effects of dietary supplementation with *S. muticum* collected from the Moroccan Atlantic coast on histological alterations in vital organs of obese Wistar rats.

2. Materials and Methods

2.1. Algal Material

Samples of the brown seaweed *Sargassum muticum* (Phylum: Ochrophyta, Class: Phaeophyceae, Order: Fucales, Family: Sargassaceae) were collected from the coast of Sidi Bouzid, Morocco, in April and June 2022 (33°13′52″ N, 8°32′51″ W). For taxonomic nomenclature, the online databases Index Nominum Algarum and AlgaeBase were consulted [7]. The algae were harvested manually and rinsed on site to remove impurities such as salt, sand, and epiphytes. After refrigerated transport, the samples were processed in the laboratory by rinsing with freshwater, followed by air-drying in the shade. Once dried, the algae were ground into a fine powder and stored at −20 °C until further use in biological experiments.

2.2. Animal Material

Thirty-five male Wistar rats, weighing between 140 and 200 g, were used in this study. The animals were housed under standard environmental conditions: temperature of 20 ± 2 °C, relative humidity of 60 ± 5%, and a 12 h light/dark cycle. Food and water were provided *ad libitum*. The study was conducted in accordance with international ethical guidelines for the use of laboratory animals and was approved by the Biomedical Research Ethics Committee of Casablanca, Morocco under approval number (No. 10/24).

2.3. Induction of Obesity

Obesity was induced in rats by administering a cafeteria diet (CAF) for a period of eight weeks. This diet consisted of a 50/50 mixture of standard chow and a high-calorie mix rich in fats and sugars, including sausage, pâté, biscuits, cheese, chips, peanut butter, and chocolate, as described by Darimont et al. [8]. The standard chow was provided by INAAM, Casablanca, Morocco. The daily ration consisted of 30 g of this mixture, prepared as a paste, dried, and administered to the animals. The nutritional composition of the diets is summarized in Table 1.

Table 1. Nutritional composition of the standard and cafeteria diets.

Diet	Proteins (g)	Carbohydrates (g)	Lipids (g)
Standard	15.5	58	2
Cafeteria	14.5	41.7	15.35

2.4. Animal Treatment

The rats were randomly divided into five experimental groups, each consisting of seven animals, and were treated for a period of two months. The first group, serving as the healthy control, received a standard diet. The second group was fed a CAF to induce obesity without any treatment. The third and fourth groups, consisting of obese rats, were treated with a CAF supplemented with 10% and 20% *S. muticum*, respectively. The fifth group, also obese, received oral treatment with orlistat at a dose of 30 mg/kg body weight [9], alongside the cafeteria diet. All diets were administered in pellet form throughout the experimental period. The 10% and 20% inclusion levels of *S. muticum* were selected based on previous studies demonstrating the efficacy and safety of similar dietary incorporation percentages, as well as on our complementary study (currently under submission) confirming good tolerance and absence of toxicity in the same experimental model.

2.5. Organ Collection and Sacrifice

At the end of the experiment (8 weeks), the rats were anesthetized by inhalation of 10% chloroform and sacrificed by decapitation after a 12 h fast. The liver, heart, brain, intestine, kidneys, pancreas, stomach, lungs, and testes were carefully removed, rinsed in 0.9% NaCl solution, and preserved in fixative for histological analysis.

2.6. Histopathological Analysis

The nine organs evaluated in this study (liver, heart, brain, intestine, kidneys, pancreas, stomach, lungs, and testes) were selected based on their known involvement and susceptibility to obesity-induced tissue alterations, allowing a comprehensive assessment of multi-organ histopathological effects of *S. muticum* treatment. The collected vital organs were fixed in 10% neutral buffered formalin. The fixed tissues were dehydrated in a graded ethanol series, embedded in paraffin, sectioned at 5 µm thickness using a microtome, deparaffinized, mounted on slides, stained with hematoxylin and eosin (H&E), and examined under a light microscope for histopathological observations. Histopathological evaluation was performed using a semi-quantitative descriptive approach based on previously reported criteria. Tissue alterations were assessed according to the presence and severity of lesions, including inflammatory infiltration, cellular degeneration, tissue disorganization, and structural damage. For each organ, multiple non-overlapping microscopic fields (at least 5–10 fields per section) were examined at different magnifications. Observations were carried out in a blinded manner to reduce observer bias. Due to the qualitative and descriptive nature of the histological assessment, results were reported descriptively

without numerical scoring, and comparisons between experimental groups were based on consistent morphological criteria observed across multiple fields.

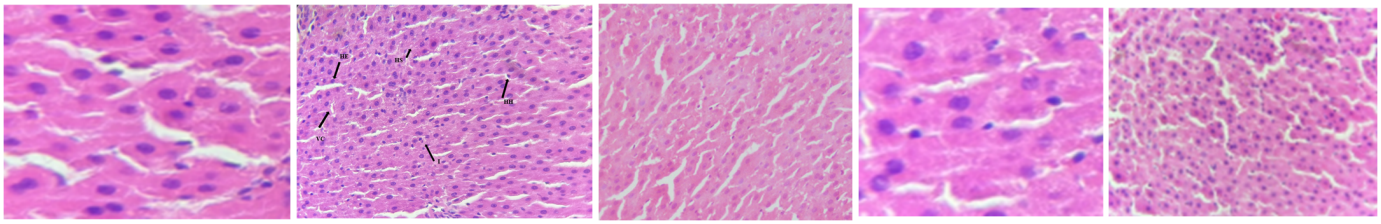
3. Results

3.1. Effect of Sargassum muticum Treatment on the Histopathology of Vital Organs

Histopathological observations were conducted on the liver, heart, brain, intestine, kidneys, pancreas, stomach, lungs, and testes to evaluate the tissue alterations induced by the cafeteria diet and the effects of *S. muticum* treatment.

3.1.1. Histopathological Effect of the Treatment on the Liver

Histological sections of the liver from the standard control group showed normal architecture (Figure 1a). In contrast, the cafeteria diet (CAF) group exhibited hepatic steatosis, blood vessel congestion, inflammation, hepatocyte hypertrophy, and hepatic edema (Figure 1b). Treatment with *S. muticum* at 10% (Figure 1c) partially restored liver structure, with noticeable reduction in steatosis and vascular congestion, though some inflammatory infiltration and hepatocyte hypertrophy persisted. In the group treated with *S. muticum* at 20% (Figure 1d), liver sections showed more advanced structural recovery, with marked reduction of steatosis, minimal inflammatory infiltration, decreased vascular congestion, and hepatocytes exhibiting normal morphology. However, in rats treated with Orlistat at 30 mg/kg, hepatic alterations were only partially reversed. Moderate hepatic steatosis persisted, along with vascular congestion, residual inflammatory infiltration, hepatic edema, and noticeable hepatocyte hypertrophy (Figure 1e).

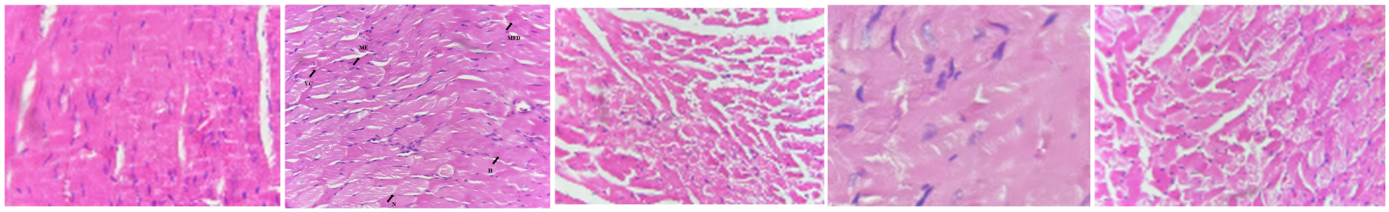


(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 1. Histological liver sections from rats in the five experimental groups: (**a**) standard group; (**b**) cafeteria diet (CAF) group; (**c**) *S. muticum* treated group (10%); (**d**) *S. muticum* treated group (20%); (**e**) Orlistat treated group (30 mg/kg). Sections were stained with H&E and observed under a 40× objective. Histopathological alterations are annotated as follows: hepatic steatosis (HS), vascular congestion (VC), inflammation (I), hepatocyte hypertrophy (HH) and hepatic edema (HE).

3.1.2. Histopathological Effect of the Treatment on the Heart

Histological examination of cardiac tissue from the standard control group revealed no pathological alterations (Figure 2a). In contrast, heart tissue from the CAF group showed blood vessel congestion, myocardial fiber degeneration, hypertrophy, necrosis, and myocardial edema (Figure 2b). Treatment with *S. muticum* at 10% (Figure 2c) improved cardiac structure, with reduction of congestion and edema, though some mild fiber degeneration persisted. In the 20% *S. muticum*-treated group (Figure 2d), cardiac tissue exhibited more complete restoration, with minimal congestion, absence of necrosis, and cardiomyocytes displaying normal morphology. In comparison, the orlistat-treated group (Figure 2e) showed only partial reversal of lesions, with persistent vascular congestion, moderate hypertrophy, and residual degeneration.

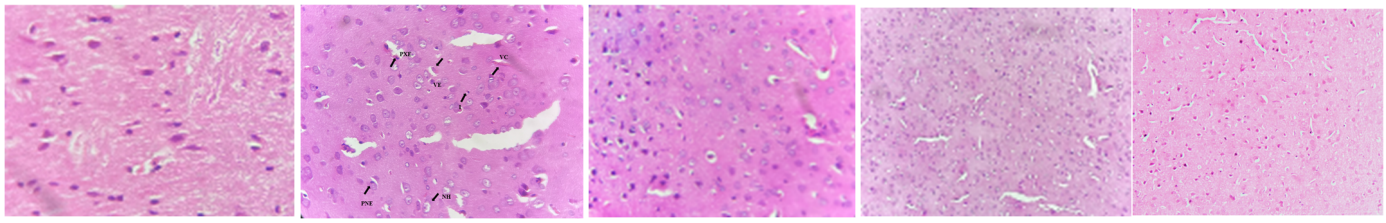


(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 2. Histological heart sections from rats in the five experimental groups: (**a**) standard group; (**b**) cafeteria diet (CAF) group; (**c**) *S. muticum* treated group (10%); (**d**) *S. muticum* treated group (20%); (**e**) Orlistat treated group (30 mg/kg). Sections were stained with H&E and observed under a 40× objective. Histopathological alterations are annotated as follows: vascular congestion (VC), myocardial fiber degeneration (MFD), hypertrophy (H), necrosis (N), myocardial edema (ME).

3.1.3. Histopathological Effect of the Treatment on the Brain

Brain sections from the control animals displayed normal tissue organization (Figure 3a). In contrast, brain tissue from the CAF group showed vascular congestion, infiltration of inflammatory cells, neuronal hypertrophy, as well as vasogenic, perineuronal and periaxonal edema (Figure 3b). In rats treated with *S. muticum* at 10% (Figure 3c), most lesions were attenuated, although slight residual edema persisted. The 20% *S. muticum* group (Figure 3d) exhibited a more complete restoration of brain architecture, with absence of edema and preservation of neuronal structure. Conversely, the orlistat-treated group (Figure 3e) showed persistent vascular congestion, neuronal hypertrophy and edema, indicating a lack of histological improvement.

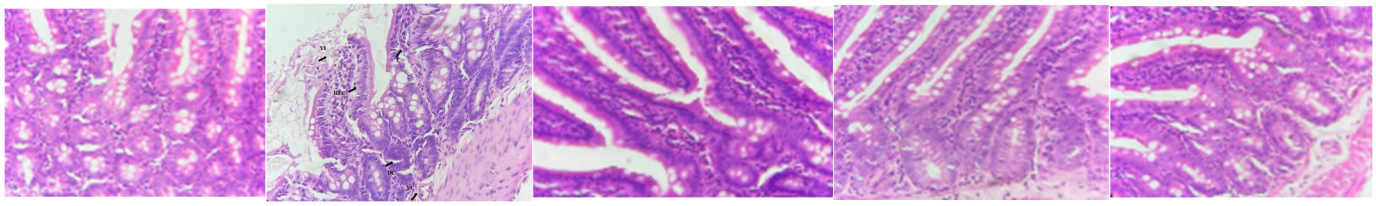


(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 3. Histological brain sections from rats in the five experimental groups: (**a**) standard group; (**b**) cafeteria diet (CAF) group; (**c**) *S. muticum* treated group (10%); (**d**) *S. muticum* treated group (20%); (**e**) Orlistat treated group (30 mg/kg). Sections were stained with H&E and observed under a 40× objective. Histopathological alterations are annotated as follows: vascular congestion (VC), inflammation (I), neuronal hypertrophy (NH), vasogenic edema (VE), perineuronal edema (PNE), and periaxonal edema (PXE).

3.1.4. Histopathological Effect of the Treatment on the Intestine

The intestinal structure appeared unchanged, with no histopathological signs observed in the standard control group (Figure 4a). In contrast, intestinal sections from the CAF group revealed vascular congestion, inflammation, hypertrophied epithelial cells, irregular villi, and disoriented crypts (Figure 4b). Treatment with *S. muticum* at 10% led to a substantial reduction of these abnormalities, with restoration of villus structure and overall mucosal organization (Figure 4c). The 20% dose resulted in a complete normalization of intestinal architecture, with no residual signs of congestion, inflammation, or epithelial hypertrophy (Figure 4d). However, the group treated with orlistat at 30 mg/kg retained the lesions observed in the CAF group (Figure 4e).

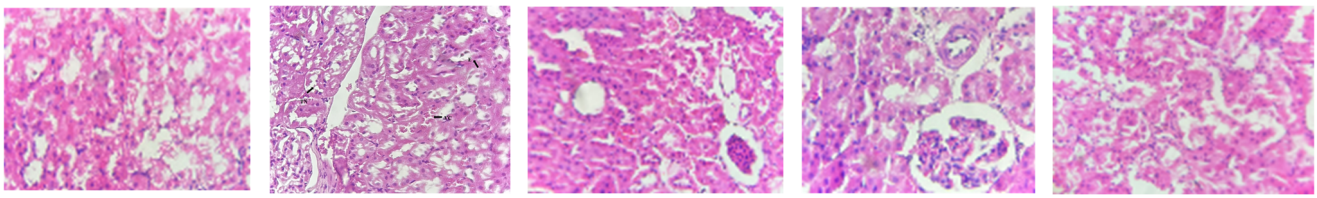


(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 4. Histological intestinal sections from rats in the five experimental groups: (**a**) standard group; (**b**) cafeteria diet (CAF) group; (**c**) *S. muticum* treated group (10%); (**d**) *S. muticum* treated group (20%); (**e**) Orlistat treated group (30 mg/kg). Sections were stained with H&E and observed under a 40× objective. Histopathological alterations are annotated as follows: vascular congestion (VC), inflammation (I), hypertrophied epithelial cells (HEC), irregular villi (IV) and disoriented crypts (DC).

3.1.5. Histopathological Effect of the Treatment on the Kidneys

The kidneys of rats in the control group exhibited normal histology (Figure 5a). In the CAF group, vascular congestion, tubular necrosis and edema were observed, without involvement of the Bowman's capsule (Figure 5b). Treatment with *S. muticum* at 10% markedly reduced these abnormalities, with restoration of tubular structure and attenuation of congestion and edema (Figure 5c). The 20% dose provided a complete normalization of renal morphology, with fully preserved glomeruli and tubules and absence of residual lesions (Figure 5d), whereas the group treated with orlistat at 30 mg/kg did not reverse the induced lesions (Figure 5e).



(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 5. Histological kidney sections from rats in the five experimental groups: (**a**) standard group; (**b**) cafeteria diet (CAF) group; (**c**) *S. muticum*-treated group (10%); (**d**) *S. muticum* treated group (20%); (**e**) Orlistat treated group (30 mg/kg). Sections were stained with H&E and observed under a 40× objective. Histopathological alterations are annotated as follows: vascular congestion (VC), tubular necrosis (TN) and edema (E).

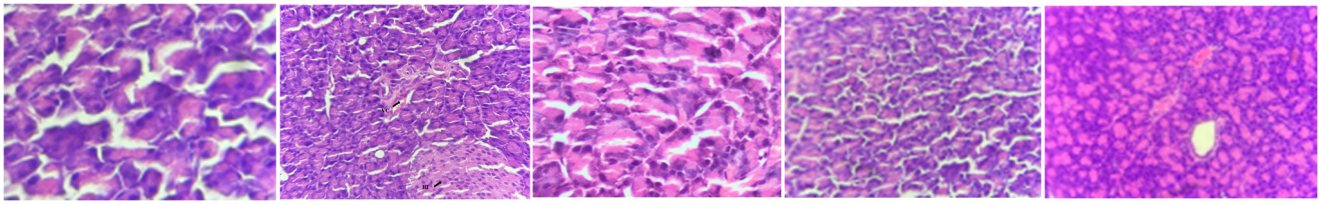
3.1.6. Histopathological Effect of the Treatment on the Pancreas

The control group showed a healthy pancreas with no evidence of damage (Figure 6a). In contrast, the CAF group exhibited pancreatic vascular congestion and hypertrophied islets (Figure 6b). Treatment with *S. muticum* at 10% resulted in a substantial reduction of these abnormalities, with restoration of pancreatic tissue organization (Figure 6c). The 20% dose led to a complete normalization of pancreatic morphology, with well-preserved acinar and islet structures and absence of congestion (Figure 6d). The group treated with orlistat at 30 mg/kg displayed the same histopathological changes as the CAF group (Figure 6e).

3.1.7. Histopathological Effect of the Treatment on the Stomach

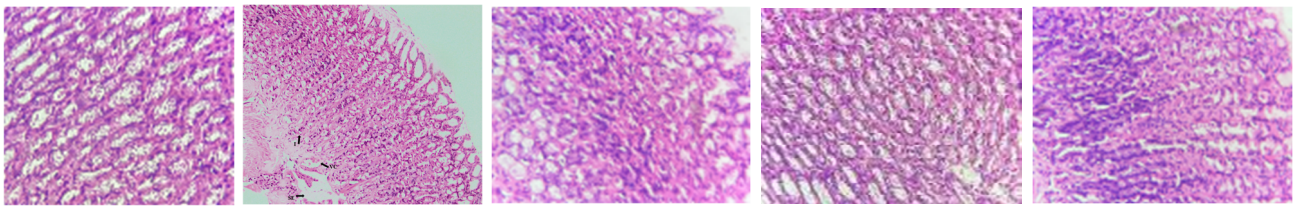
The stomachs of rats in the standard control group exhibited normal histological structure (Figure 7a). Histopathological analysis of the stomachs from the CAF group revealed vascular congestion, inflammation and submucosal edema (Figure 7b). Treatment with *S. muticum* at 10% markedly reduced these lesions, restoring gastric tissue organization (Figure 7c). The 20% dose produced an even greater effect, leading to complete normalization of the gastric structure with absence of congestion, inflammation, or edema (Figure 7d).

However, rats treated with orlistat at 30 mg/kg retained the lesions observed in the CAF group, indicating persistent gastric damage (Figure 7e).



(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 6. Histological pancreatic sections from rats in the five experimental groups: (**a**) standard group; (**b**) cafeteria diet (CAF) group; (**c**) *S. muticum* treated group (10%); (**d**) *S. muticum* treated group (20%); (**e**) Orlistat-treated group (30 mg/kg). Sections were stained with H&E and observed under a 40× objective. Histopathological alterations are annotated as follows: vascular congestion (VC) and hypertrophied islets (HI).

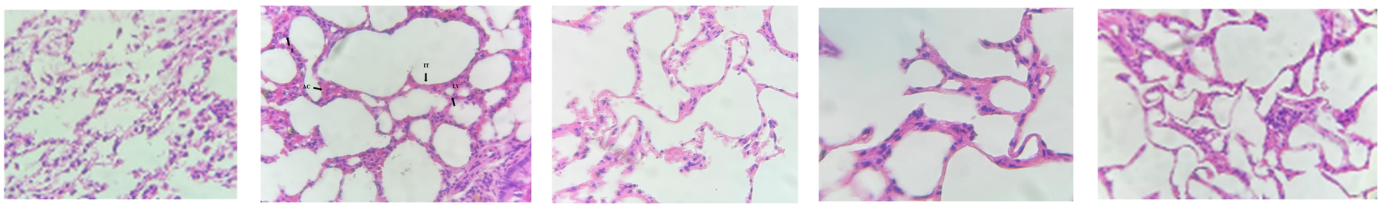


(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 7. Histological stomach sections from rats in the five experimental groups: (**a**) standard group; (**b**) cafeteria diet (CAF) group; (**c**) *S. muticum* treated group (10%); (**d**) *S. muticum* treated group (20%); (**e**) Orlistat-treated group (30 mg/kg). Sections were stained with H&E and observed under a 40× objective. Histopathological alterations are annotated as follows: vascular congestion (VC), inflammation (I) and submucosal edema (SE).

3.1.8. Histopathological Effect of the Treatment on the Lungs

Histological examination of the lungs from the standard control group revealed normal architecture (Figure 8a). In contrast, lungs from the CAF group showed alveolar congestion, inflammation, interstitial thickening and lipid vacuoles (Figure 8b). Treatment with *S. muticum* at 10% partially improved lung histology, with reduced congestion and edema (Figure 8c), whereas the 20% dose fully restored normal pulmonary architecture (Figure 8d). In contrast, rats treated with orlistat at 30 mg/kg still showed persistent lesions similar to those in the CAF group (Figure 8e).



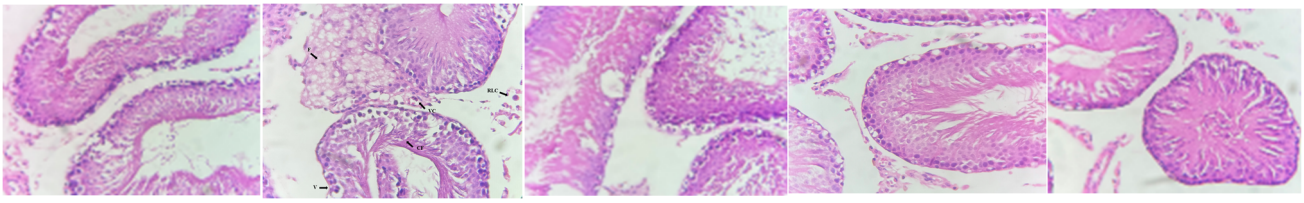
(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 8. Histological lung sections from rats in the five experimental groups: (**a**) standard group; (**b**) cafeteria diet (CAF) group; (**c**) *S. muticum* treated group (10%); (**d**) *S. muticum* treated group (20%); (**e**) Orlistat-treated group (30 mg/kg). Sections were stained with H&E and observed under a 40× objective. Histopathological alterations are annotated as follows: alveolar congestion (AC), inflammation (I), interstitial thickening (IT) and lipid vacuoles (LV).

3.1.9. Histopathological Effect of the Treatment on the Testes

The testicular architecture in the control rats was normal (Figure 9a). In contrast, the CAF diet induced fibrosis, vacuolization, vascular congestion, a reduction in Leydig cells

and cyst formation (Figure 9b). Treatment with *S. muticum* at 10% partially improved testicular histology, with reduced fibrosis and vacuolization (Figure 9c), whereas the 20% dose fully restored normal testicular organization (Figure 9d). The group treated with orlistat at 30 mg/kg did not prevent these alterations (Figure 9e).



(**a**) (**b**) (**c**) (**d**) (**e**)

Figure 9. Histological testicular sections from rats in the five experimental groups: (**a**) standard group; (**b**) cafeteria diet (CAF) group; (**c**) *S. muticum* treated group (10%); (**d**) *S. muticum* treated group (20%); (**e**) Orlistat-treated group (30 mg/kg). Sections were stained with H&E and observed under a 40× objective. Histopathological alterations are annotated as follows: fibrosis (F), vacuolization (V), vascular congestion (VC), reduction in Leydig cells (RLC) and cyst formation (CF).

4. Discussion

Obesity is a chronic, multifactorial pathology involving systemic metabolic, endocrine, and inflammatory disturbances. It acts as a catalyst for various comorbidities through interconnected mechanisms including low-grade chronic inflammation, oxidative stress, insulin resistance, and alterations of the gut microbiota [10,11]. In our study, the cafeteria diet (CAF)-induced obese rat model successfully reproduced major histopathological complications associated with this condition. Treatment with *Sargassum muticum* demonstrated a protective effect at multiple levels, suggesting a multidimensional therapeutic potential.

Obesity leads to hepatic lipid overload through excessive fatty acid supply, activating lipogenic pathways such as SREBP-1c and ChREBP while inhibiting hepatic β-oxidation [12]. This results in NAFLD, as evidenced by steatosis, hepatocyte hypertrophy, and vascular congestion observed in our CAF group. These alterations correspond to the activation of M1-type macrophages in the liver, which secrete pro-inflammatory cytokines (TNF-α, IL-1β), contributing to progression towards steatohepatitis [13]. Treatment with *S. muticum* led to marked histological improvement of the liver, with reduced steatosis and congestion lesions. This benefit may be explained by several complementary mechanisms: activation of the AMPK pathway, which inhibits lipogenic factors SREBP-1c and ChREBP while stimulating β-oxidation; reduction of hepatic oxidative stress through scavenging of reactive oxygen species by fucoidans and polyphenols; and improved hepatic insulin sensitivity by enhancing signaling via the IRS-1/PI3K/Akt pathway. These effects converge to better regulation of lipid metabolism and prevention of progression to steatohepatitis [14–18].

The identified myocardial lesions (necrosis, edema, degeneration) reflect pathological cardiac remodeling induced by obesity. This phenomenon is associated with endoplasmic reticulum stress activation, production of free radicals by NADPH oxidases, and myocardial fibrosis [19]. The heart progressively becomes insensitive to insulin and growth factors, promoting cardiomyocyte apoptosis. The cardioprotective role of *S. muticum* may be explained by the reduction of mitochondrial oxidative stress and modulation of the PI3K/Akt and MAPK/ERK pathways, as demonstrated with fucoxanthin in cardiac models exposed to lipid stress. Indeed, marine polyphenols and carotenoids such as fucoxanthin present in *S. muticum* act as potent antioxidants by neutralizing reactive oxygen species (ROS) generated by dysfunctional mitochondria. This activity helps preserve cardiomyocyte integrity by limiting mitochondrial DNA damage and lipid membrane peroxidation. Moreover, *S. muticum* activates the PI3K/Akt pathway, promoting cell survival, phosphorylation of GSK-3β, and

inhibition of Bax/Bcl-2-mediated apoptosis. Simultaneously, regulation of the MAPK/ERK pathway contributes to reducing myocardial inflammation and preventing cardiac fibrosis by inhibiting the expression of TGF-β1 and collagens I/III, key elements of pathological remodeling [20]. These convergent mechanisms indicate a potential role of *S. muticum* in preventing cardiovascular complications of obesity, notably metabolic cardiomyopathy.

At the cerebral level, obesity-induced neuroinflammation results from the passage of pro-inflammatory cytokines across the blood–brain barrier, leading to microglial activation and neuronal damage [21,22]. We observed neuronal hypertrophy, vasogenic edema, and cellular infiltration. These alterations are similar to mechanisms involved in neurodegenerative diseases such as Alzheimer's disease, where the obesity–insulin resistance axis plays a central role. *S. muticum*, rich in neuroprotective compounds, may inhibit the production of nitric oxide (NO) and neurotoxic cytokines, thereby attenuating microglial activation, according to recent studies on the effects of marine polysaccharides [23]. This action is thought to occur primarily through inhibition of pro-inflammatory signaling pathways such as NF-κB and JNK/p38 MAPK, which are activated in microglial cells exposed to lipopolysaccharides or amyloid deposits [24]. Phlorotannins and fucoidans derived from *S. muticum* have been shown to reduce the expression of pro-inflammatory enzymes like iNOS and COX-2, thereby decreasing the production of NO and PGE2, which contribute to neuroinflammation and neurotoxicity [25]. Together, these mechanisms support the neuroprotective potential of *S. muticum*, especially relevant in the context of obesity, where the blood–brain barrier is compromised and neuroinflammation is exacerbated.

The intestine plays a pivotal role in the development of obesity through altered intestinal permeability, bacterial translocation, and dysbiosis. These phenomena induce systemic metabolic inflammation by activating TLR4 receptors and increasing circulating lipopolysaccharides [26]. The intestinal lesions observed, villus atrophy and crypt disorganization, confirm this imbalance. *S. muticum* appears to restore epithelial integrity, possibly by stimulating beneficial bacteria such as *Akkermansia muciniphila* and reducing pro-inflammatory Enterobacteriaceae, as reported in murine models treated with algae rich in fibers and sulfated polysaccharides [27]. Additionally, fucoidans and other polysaccharides from *S. muticum* may strengthen tight junction proteins (occludin, claudin-1, ZO-1), thereby reducing intestinal permeability and limiting endotoxin translocation [28]. These compounds also promote the local production of short-chain fatty acids (SCFAs), notably butyrate, which functions as an immunomodulator and fuel for epithelial cells, contributing to mucosal regeneration [29]. Furthermore, some studies indicate that phlorotannins from *S. muticum* can inhibit activation of the TLR4/NF-κB pathways in intestinal epithelium, reducing the local production of pro-inflammatory cytokines (TNF-α, IL-6) [30]. Together, these mechanisms could explain the reduction of intestinal inflammation and restoration of mucosal homeostasis observed in the treated groups.

The documented renal lesions (tubular necrosis, congestion) fall within the scope of metabolic nephropathy, where glomerular hyperfiltration and lipotoxicity induce local inflammation, promoted by NF-κB activation and MCP-1 production [31]. The protective effects of *S. muticum* may result from inhibition of these inflammatory and fibrotic cascades. Indeed, sulfated polysaccharides and phlorotannins present in the alga have been reported to inhibit nuclear translocation of NF-κB, reduce the expression of pro-inflammatory genes, and attenuate TGF-β1 activation, thereby limiting the development of renal fibrosis [32]. Moreover, some studies have shown that brown algae extracts favorably modulate the renin–angiotensin–aldosterone system (RAAS) by reducing angiotensin converting enzyme (ACE) activity, which could alleviate glomerular hypertension and preserve renal function in models of induced nephrotoxicity [33]. These combined mechanisms may explain the histological preservation observed in the renal cortex of groups treated with *S. muticum*.

The pancreas, a key organ in glycemic regulation, undergoes adaptive alterations in response to nutritional overload. The hypertrophy of the islets of Langerhans observed in CAF rats illustrates beta-cell hyperstimulation, often followed by functional exhaustion. This phenomenon is linked to oxidative stress activation, endoplasmic reticulum stress pathways, and increased IL-1β production [34]. The preservation of pancreatic structure in treated groups suggests that *S. muticum* could improve insulin sensitivity via activation of the IRS-1/PI3K/Akt pathway and reduction of intra-islet IL-1β, as demonstrated in previous studies on brown macroalgae [35–37].

In rats subjected to the cafeteria diet, notable histopathological alterations were observed in the stomach and lungs, reflecting a marked systemic inflammatory state. The stomach exhibited vascular congestion, submucosal edema, and inflammatory infiltration, while the lungs showed alveolar congestion, interstitial thickening, lipid vacuoles, and hemorrhagic foci. These lesions are consistent with immune system activation induced by excess adipose tissue, particularly via hyperleptinemia, which is known to stimulate pro-inflammatory cytokine production and activate neutrophils [38,39]. Treatment with *S. muticum* led to near-complete restoration of the histological architecture of these organs, indicating a clear anti-inflammatory effect. This potential may be attributed to the richness of this alga in bioactive compounds, notably phlorotannins, which can inhibit TLR receptor signaling and modulate inflammatory pathways such as NF-κB and MAPK [40]. Furthermore, fucoxanthin, a carotenoid pigment present in *S. muticum*, has been shown in several studies to reduce COX-2 expression by inhibiting p38 MAPK and JNK phosphorylation, thereby limiting the production of pro-inflammatory prostaglandins (PGE2) [41]. Recent research has also confirmed the anti-inflammatory effects of *S. muticum* in various experimental models, with significant reductions in TNF-α, IL-6, and IL-1β levels both in the intestine and lungs [42]. These observations support our findings and suggest that the protective effect of *S. muticum* against gastric and pulmonary lesions may result from a broad-spectrum anti-inflammatory action.

Finally, the testicular alterations (atrophy, vacuolization, fibrosis) are characteristic of functional hypogonadism related to obesity, resulting from increased tissue aromatase activity and leptin resistance [43]. This condition decreases testosterone production and impairs spermatogenesis [44]. The protective role of *S. muticum* could be explained by the inhibition of oxidative stress in Sertoli and Leydig cells, as demonstrated in models of testicular toxicity mitigated by brown algae extracts [45,46].

Overall, *S. muticum* attenuated obesity-induced histopathological lesions across multiple organs, suggesting a multi-organ protective activity. These observations align with recent data on brown macroalgae, known for their antioxidant, anti-inflammatory, and metabolic regulatory effects [47,48].

In a complementary study is currently under submission, we characterized the biochemical composition of *Sargassum muticum*, revealing a profile dominated by carbohydrates (25.45%), followed by proteins (5.89%) and lipids (2%). These values are consistent with those reported for *S. muticum* in the literature and highlight its richness in polysaccharides, supporting its potential as a functional food [4,49,50]. In the same study, the treatment with *S. muticum* was also associated with an improvement in the lipid profile and several metabolic markers related to obesity. The present work provides histopathological evidence that complements these physiological and biochemical findings, further illustrating the multi-level protective effects of *S. muticum* against obesity-induced organ damage.

A key finding of this study is that S. muticum at the 20% supplementation level exerted more pronounced histoprotective effects than the 10% dose and even surpassed orlistat, a standard anti-obesity treatment. While orlistat primarily acts by reducing lipid absorption [51], the multi-target bioactive profile of *S. muticum* notably its phlorotannins, fucoxan-

thin, and sulfated polysaccharides appears to confer broader systemic protection, including attenuation of inflammation and normalization of tissue architecture [50]. This suggests that *S. muticum* not only mimics but may also surpass the therapeutic effects of pharmacological intervention, highlighting its potential as a natural and effective alternative.

Beyond the biomedical perspective, this study underscores the sustainable valorization of *S. muticum*, an invasive species that poses ecological challenges along the Moroccan Atlantic coast [4]. By transforming this problematic alga into a therapeutic resource, our findings provide a dual benefit: contributing to the mitigation of ecological impacts while offering a novel nutraceutical strategy against obesity and its complications. This approach exemplifies how marine biodiversity can be harnessed for human health while promoting environmental and socio-economic sustainability.

5. Conclusions

Cafeteria diet-induced obesity caused multivisceral histopathological alterations reflecting the severity of damage associated with this chronic condition. Our study demonstrated that treatment with *S. muticum* significantly attenuates these lesions in the liver, heart, brain, intestine, kidneys, pancreas, lungs, stomach, and testes, suggesting an overall protective role and supporting the potential of this macroalga in preventing obesity-related organ complications. However, this study has limitations, including the absence of long-term follow-up, the use of an animal model, and the lack of human-relevant biomarkers. These experimental findings call for further studies to better characterize its bioactive compounds, develop nutraceutical formulations, and conduct pilot clinical trials to assess safety and efficacy in humans, facilitating the translation of preclinical results into potential therapeutic applications.

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Data Availability Statement: The data presented in this study is contained within the article.

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References

1. Karkour, T.A.; Abd Aldayem, T.; Abd El Aziz Ibrahim, T.M.; Ally, N.M. Fetal malformations and maternal obesity: A cross-sectional study at El Shatby University Maternity Hospital. *ALEXMED ePosters* **2024**, *6*, 48–49. [CrossRef]
2. Jin, X.; Qiu, T.; Li, L.; Yu, R.; Chen, X.; Li, C.; Jiang, T. Pathophysiology of obesity and its associated diseases. *Acta Pharm. Sin. B* **2023**, *13*, 2403–2424. [CrossRef]
3. Fonseca-Barahona, I.; Shahbaz, K.; Baroutian, S. Bioactives from brown algae: Antioxidant, anti-inflammatory, anticancer, and antimicrobial potential. *ChemBioEng Rev.* **2025**, *12*, e70007. [CrossRef]

4. Aamiri, A.; Lahcen, T.O.B.; Pereira, L.; Benhniya, B.; Zidane, H.; Rezzoum, N.E. Spatiotemporal variation in phenology of the invasive brown macroalga *Sargassum muticum* (Yendo) Fensholt and the environmental parameter relationships along four different sites on the Atlantic coast of Morocco. *Algal Res.* **2024**, *81*, 103576. [CrossRef]
5. Aamiri, A.; Rezzoum, N.E.; Touhamia, Y.; Zidane, H.; Benhassan, L.; Pascal, P.Y.; Lahcen, T.O.B. Seasonal variation in biochemical and metal content of the invasive seaweed *Sargassum muticum* along the Moroccan Atlantic coast. *J. Appl. Phycol.* **2024**, *36*, 2383–2394. [CrossRef]
6. El Atouani, S.; Bentiss, F.; Reani, A.; Zrid, R.; Belattmania, Z.; Pereira, L.; Sabour, B. The invasive brown seaweed *Sargassum muticum* as a new resource for alginate in Morocco: Spectroscopic and rheological characterization. *Phycol. Res.* **2016**, *64*, 185–193. [CrossRef]
7. Guiry, M.D.; Guiry, G.M. *AlgaeBase*; World-Wide Electronic Publication, National University of Ireland: Galway, Ireland, 2025. Available online: https://www.algaebase.org (accessed on 28 February 2026).
8. Darimont, C.; Turini, M.; Epitaux, M.; Zbinden, I.; Richelle, M.; Montell, E.; Ferrer-Martinez, A.; Macé, K. β3-adrenoceptor agonist prevents alterations of muscle diacylglycerol and adipose tissue phospholipids induced by a cafeteria diet. *Nutr. Metab.* **2004**, *1*, 4. [CrossRef]
9. Kolsi, R.B.A.; Salah, H.B.; Jardak, N.; Chaaben, R.; Jribi, I.; El Feki, A.; Belghith, K. Sulphated polysaccharide isolated from *Sargassum vulgare*: Characterization and hypolipidemic effects. *Carbohydr. Polym.* **2017**, *170*, 148–159. [CrossRef] [PubMed]
10. Hotamisligil, G.S. Inflammation, metaflammation and immunometabolic disorders. *Nature* **2017**, *542*, 177–185. [CrossRef] [PubMed]
11. Saltiel, A.R.; Olefsky, J.M. Inflammatory mechanisms linking obesity and metabolic disease. *J. Clin. Investig.* **2017**, *127*, 1–4. [CrossRef]
12. Samuel, V.T.; Shulman, G.I. Nonalcoholic fatty liver disease as a nexus of metabolic and hepatic diseases. *Cell Metab.* **2018**, *27*, 22–41. [CrossRef]
13. Buzzetti, E.; Pinzani, M.; Tsochatzis, E.A. The multiple-hit pathogenesis of non-alcoholic fatty liver disease (NAFLD). *Metabolism* **2016**, *65*, 1038–1048. [CrossRef] [PubMed]
14. Shih, P.H.; Shiue, S.J.; Chen, C.N.; Cheng, S.W.; Lin, H.Y.; Wu, L.W.; Wu, M.S. Fucoidan and fucoxanthin attenuate hepatic steatosis and inflammation of NAFLD through modulation of leptin/adiponectin axis. *Mar. Drugs* **2021**, *19*, 148. [CrossRef]
15. Yang, S.; Li, J.; Yan, L.; Wu, Y.; Zhang, L.; Li, B.; Tong, H.; Lin, X. Molecular mechanisms of fucoxanthin in alleviating lipid deposition in metabolic associated fatty liver disease. *J. Agric. Food Chem.* **2024**, *72*, 10391–10405. [CrossRef] [PubMed]
16. Chu, X.; Wang, X.; Feng, K.; Bi, Y.; Xin, Y.; Liu, S. Fucoidan ameliorates lipid accumulation, oxidative stress, and NF-κB-mediated inflammation by regulating the PI3K/AKT/Nrf2 signaling pathway in a free fatty acid-induced NAFLD spheroid model. *Lipids Health Dis.* **2025**, *24*, 55. [CrossRef] [PubMed]
17. Zhao, W.; Shen, Y.; Bao, Y.; Monroig, Ó.; Zhu, T.; Sun, P.; Tocher, D.R.; Zhou, Q.; Jin, M. Fucoidan alleviates hepatic lipid deposition by modulating the Perk-Eif2α-Atf4 axis via Sirt1 activation in *Acanthopagrus schlegelii*. *Int. J. Biol. Macromol.* **2024**, *282*, 137266. [CrossRef]
18. Liu, Y.; Zhang, D.; Liu, G.M.; Chen, Q.; Lu, Z. Ameliorative effect of dieckol-enriched extraction from Laminaria japonica on hepatic steatosis induced by a high-fat diet via β-oxidation pathway in ICR mice. *J. Funct. Foods* **2019**, *58*, 44–55. [CrossRef]
19. Zhang, Y.; Zhang, R.J. Obesity-induced cardiac remodeling and dysfunction. *Obes. Rev.* **2020**, *21*, e12934. [CrossRef]
20. Zhang, Q.; Jin, A.; Cheng, H.; Li, S.; Li, W. Fucoxanthin attenuates myocardial ischemia/reperfusion-induced injury via AMPK/GSK-3β/Nrf2 axis. *Chem. Biol. Drug Des.* **2024**, *104*, e14621. [CrossRef]
21. Guillemot-Legris, O.; Muccioli, G.G. Obesity-induced neuroinflammation: Beyond the hypothalamus. *Trends Neurosci.* **2017**, *40*, 237–253. [CrossRef]
22. Le Thuc, O.; García-Cáceres, C. Obesity-induced inflammation: Connecting the periphery to the brain. *Nat. Metab.* **2024**, *6*, 1237–1252. [CrossRef]
23. Patil, N.P.; Le, V.; Sligar, A.D.; Mei, L.; Chavarria, D.; Yang, E.Y.; Baker, A.B. Algal polysaccharides as therapeutic agents for atherosclerosis. *Front. Cardiovasc. Med.* **2018**, *5*, 153. [CrossRef] [PubMed]
24. Wang, Y.; Wang, Q.; Duan, L.; Li, X.; Yang, W.; Huang, T.; Kong, M.; Guan, F.; Ma, S. Fucoidan ameliorates LPS-induced neuronal cell damage and cognitive impairment in mice. *Int. J. Biol. Macromol.* **2022**, *222*, 759–771. [CrossRef] [PubMed]
25. Jannat, K.; Balakrishnan, R.; Han, J.H.; Yu, Y.J.; Kim, G.W.; Choi, D.K. The neuropharmacological evaluation of seaweed: A potential therapeutic source. *Cells* **2023**, *12*, 2652. [CrossRef]
26. Wang, K.; Lai, W.; Min, T.; Wei, J.; Bai, Y.; Cao, H.; Guo, J.; Su, Z. The effect of enteric-derived lipopolysaccharides on obesity. *Int. J. Mol. Sci.* **2024**, *25*, 4305. [CrossRef]

27. Lee, Z.J.; Xie, C.; Ng, K.; Suleria, H.A. Unraveling the bioactive interplay: Seaweed polysaccharide, polyphenol and their gut modulation effect. *Crit. Rev. Food Sci. Nutr.* **2025**, *65*, 382–405. [CrossRef]
28. Zhu, L.; Ren, Y.; Zhang, S.; Guo, Y.; Zong, J.; Liu, Y. Marine-derived polysaccharides: The potential agents against neurodegenerative diseases. *Front. Pharmacol.* **2024**, *15*, 1506789. [CrossRef] [PubMed]
29. Wu, S.; Zuo, J.; Cheng, Y.; Zhang, Y.; Zhang, Z.; Wu, M.; Yang, Y.; Tong, H. Ethanol extract of *Sargarsum fusiforme* alleviates HFD/STZ-induced hyperglycemia in association with modulation of gut microbiota and intestinal metabolites in type 2 diabetic mice. *Food Res. Int.* **2021**, *147*, 110550. [CrossRef]
30. Besednova, N.N.; Andryukov, B.G.; Zaporozhets, T.S.; Kuznetsova, T.A.; Kryzhanovsky, S.P.; Ermakova, S.P.; Galkina, I.V.; Shchelkanov, M.Y. Molecular targets of brown algae phlorotannins for the therapy of inflammatory processes of various origins. *Mar. Drugs* **2022**, *20*, 243. [CrossRef]
31. Mao, T.H.; Huang, H.Q.; Zhang, C.H. Clinical characteristics and treatment compounds of obesity-related kidney injury. *World J. Diabetes* **2024**, *15*, 1091. [CrossRef]
32. Rizk, M.Z.; El-Sherbiny, M.; Borai, I.H.; Ezz, M.K.; Aly, H.F.; Matloub, A.A.; Farrag, A.E.-R.; Fouad, G.I. Sulphated polysaccharides (SPS) from the green alga *Ulva fasciata* extract modulates liver and kidney function in high fat diet-induced hypercholesterolemic rats. *Int. J. Pharm. Pharm. Sci.* **2016**, *8*, 43–55.
33. Sohail, N.; Farhat, H. Role of seaweeds in drug induced nephrotoxicity. *Mar. Sci. Technol. Bull.* **2022**, *11*, 515–532. [CrossRef]
34. Zhang, X.; Xu, C.; Ji, L.; Zhang, H. Endoplasmic reticulum stress in acute pancreatitis: Exploring the molecular mechanisms and therapeutic targets. *Cell Stress Chaperones* **2025**, *30*, 119–129. [CrossRef]
35. Zhang, Y.; Xu, W.; Huang, X.; Zhao, Y.; Ren, Q.; Hong, Z.; Huang, M.; Xing, X. Fucoxanthin ameliorates hyperglycemia, hyperlipidemia and insulin resistance in diabetic mice partially through IRS-1/PI3K/Akt and AMPK pathways. *J. Funct. Foods* **2018**, *48*, 515–524. [CrossRef]
36. Yu, W.-C.; Chen, Y.-L.; Hwang, P.-A.; Chen, T.-H.; Chou, T.-C. Fucoidan ameliorates pancreatic β-cell death and impaired insulin synthesis in streptozotocin-treated β cells and mice via a Sirt-1-dependent manner. *Mol. Nutr. Food Res.* **2017**, *61*, 1700136. [CrossRef] [PubMed]
37. Yang, C.F.; Lai, S.S.; Chen, Y.H.; Liu, D.; Liu, B.; Ai, C.; Wan, X.-Z.; Gao, L.-Y.; Chen, X.-H.; Zhao, C. Anti-diabetic effect of oligosaccharides from seaweed *Sargassum confusum* via JNK-IRS1/PI3K signalling pathways and regulation of gut microbiota. *Food Chem. Toxicol.* **2019**, *131*, 110562. [CrossRef]
38. Pérez-Pérez, A.; Sánchez-Jiménez, F.; Vilariño-García, T.; Sánchez-Margalet, V. Role of leptin in inflammation and vice versa. *Int. J. Mol. Sci.* **2020**, *21*, 5887. [CrossRef] [PubMed]
39. Barrara, F.S.; Ramirez, D.C.; Mejiba, S.E.G. Pulmonary neutrophilic inflammation worsens obesity-associated comorbidities. *Preprints* **2025**, 202505.1916. [CrossRef]
40. Barbosa, M.; Lopes, G.; Andrade, P.B.; Valentão, P. Bioprospecting of brown seaweeds for biotechnological applications: Phlorotannin actions in inflammation and allergy network. *Trends Food Sci. Technol.* **2019**, *86*, 153–171. [CrossRef]
41. Joung, E.J.; Cao, L.; Gwon, W.G.; Kwon, M.S.; Lim, K.T.; Kim, H.R. Meroterpenoid-rich ethanoic extract of *Sargassum macrocarpum* ameliorates dextran sulfate sodium-induced colitis in mice. *Foods* **2022**, *11*, 329. [CrossRef]
42. Fernandez, C.J.; Chacko, E.C.; Pappachan, J.M. Male obesity-related secondary hypogonadism—Pathophysiology, clinical implications and management. *Eur. Endocrinol.* **2019**, *15*, 83–90. [CrossRef]
43. Khodamoradi, K.; Khosravizadeh, Z.; Seetharam, D.; Mallepalli, S.; Farber, N.; Arora, H. The role of leptin and low testosterone in obesity. *Int. J. Impot. Res.* **2022**, *34*, 704–713. [CrossRef] [PubMed]
44. Semaida, A.I.; El-Khashab, M.A.; Saber, A.A.; Hassan, A.I.; Elfouly, S.A. Effects of *Sargassum virgatum* extracts on the testicular measurements, genomic DNA and antioxidant enzymes in irradiated rats. *Int. J. Radiat. Biol.* **2022**, *98*, 191–204. [CrossRef] [PubMed]
45. Chen, L.; Liu, R.; He, X.; Pei, S.; Li, D. Effects of brown seaweed polyphenols, a class of phlorotannins, on metabolic disorders via regulation of fat function. *Food Funct.* **2021**, *12*, 2378–2388. [CrossRef] [PubMed]
46. Wu, S.; Sui, Z.; Pan, J.; Li, X.; Xue, D.; Han, X.; Shen, Y. Phlorotannins and glycolipid metabolism: Comprehensive regulatory roles mediated by the gut microbiota. *Front. Nutr.* **2026**, *13*, 1750434. [CrossRef]
47. Wang, P.-T.; Sudirman, S.; Hsieh, M.-C.; Hu, J.-Y.; Kong, Z.-L. Oral supplementation of fucoxanthin-rich brown algae extract ameliorates cisplatin-induced testicular damage in hamsters. *Biomed. Pharmacother.* **2020**, *125*, 109992. [CrossRef]
48. Silva, A.; Soares, C.; Carpena, M.; Oliveira, P.G.; Echave, J.; Chamorro, F.; Donn, P.; Mansour, S.S.; Barroso, M.F.; Prieto, M.A. Assessment of nutritional profile of *Sargassum muticum* alga from the Spanish coastline. *Biol. Life Sci. Forum* **2023**, *26*, 94. [CrossRef]
49. Mouga, T.; Almeida, M.M.; Pitacas, F.I.; Rodrigues, A.M.; Vitória, C.; Anjos, O. Elemental and nutritional characterisation with vibrational spectroscopy analysis of *Ulva* sp., *Gracilaria multipartita*, and *Sargassum muticum*. *Appl. Sci.* **2025**, *15*, 4212. [CrossRef]

50. Uuh Narvaez, J.J.; Chan Zapata, I.; Segura Campos, M.R. Combined potential of orlistat with natural sources and their bioactive compounds against obesity: A review. *Molecules* **2025**, *30*, 2392. [CrossRef]
51. Torres-Narváez, A.; Olvera-Ramírez, A.M.; Castaño-Sánchez, K.; Chávez-Servín, J.L.; Reis de Souza, T.C.; McEwan, N.R.; Ferriz-Martínez, R.A. Therapeutic and nutraceutical potential of *Sargassum* species: A narrative review. *Mar. Drugs* **2025**, *23*, 343. [CrossRef]

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