

Natural Plant Powders for Obesity and its Complications: A Study on Watermelon Rind and Date Seed Supplementation in Rats Fed a High-Fat Diet

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Abstract This study aimed to assess the potential therapeutic effects of watermelon rind powder (WRP) and date seed powder (DSP) on obesity-related complications in rats induced by a high-fat diet (HFD), exploring their roles as natural interventions for obesity management. Thirty-six rats were divided into a normal control group (G1, 6 rats) fed a basic diet (BD) and an obesity-induced group (G2, 30 rats) fed HFD for 8 weeks. G2 was then subdivided into five groups: G2 as model control (obese rats), G3 and G4 receiving BD + WRP at 5% and 10%, respectively, and G5 and G6 receiving BD + DSP at 5% and 10%, respectively. The HFD effectively induced obesity, as evidenced by increased body weight gain (BWG), feed intake (FI), and feed efficiency ratio (FER), alongside adverse alterations in organ weights, liver and kidney function, metabolic parameters, lipid profile, oxidative stress markers, and antioxidant status. WRP and DSP both significantly mitigated these effects in a dose-dependent manner, with WRP generally showing stronger effects. WRP treatment reduced BWG by up to 31.12%, decreased FI and FER, and significantly improved liver, kidney, and heart weights. It also lowered liver enzymes (ALT, AST, ALP), improved protein profile (TP, Alb, Glb, A/G ratio), decreased GGT, and reduced bilirubin levels (TB, DB, IDB). Similarly, WRP enhanced glucose-insulin regulation by lowering blood glucose by up to 56.05% and increasing insulin by over 1000%, while also raising leptin levels. Lipid profiles improved markedly with reduced total cholesterol (T.C), triglycerides (T.G), LDL, and VLDL, and increased HDL. Kidney markers such as uric acid, urea, and creatinine also declined significantly. Moreover, WRP restored antioxidant markers like GSH, GSH-Px, CAT, and SOD, indicating reduced oxidative stress. DSP also provided notable benefits across all parameters, although its impact was generally milder than WRP's, except for some oxidative stress markers at lower doses. Overall, both WRP and DSP exhibited protective effects against obesity-induced complications, with WRP showing greater potential as a functional dietary supplement for obesity management.

Keywords: Liver enzymes, kidney functions, metabolic parameters, lipid profile, leptin, antioxidant status, histology

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1. Introduction

Excessive body fat accumulation, a condition known as obesity, is a multifaceted metabolic disorder that significantly increases the likelihood of developing serious health problems like heart disease, type 2 diabetes, unhealthy cholesterol levels, and some cancers [1]. Statistics from the World Health Organization in 2016 indicated a widespread issue, with over 1.9 billion adults classified as overweight and more than 650 million meeting the criteria for obesity [2]. The situation is even more pressing in Egypt, where recent statistics show that 39.8% of the adult population is obese, particularly among women, placing the country among the top ten globally in obesity prevalence [3]. Despite the development of various pharmacological treatments-including orlistat,

liraglutide, and semaglutide-these synthetic drugs are frequently linked to adverse outcomes, including gastrointestinal distress, pancreatitis, renal complications, and increased cardiovascular risk [4,5]. Furthermore, its elevated expense and restricted availability in low- and middle-income nations, including Egypt, underscore the need for safer, more affordable therapeutic options.

In light of these issues, there has been an increasing interest in the use of plant-based therapies as culturally acceptable, accessible, and biologically potent alternatives. Egypt's rich biodiversity offers an abundance of underutilized medicinal plants and agricultural byproducts that are naturally high in bioactive compounds, such as polyphenols, flavonoids, and dietary fiber [6]. Among these, watermelon rind and date seeds-typically considered agricultural waste-have gained attention for their potential anti-obesity properties. Both contain bioactive components like citrulline, phenolic acids, and

dietary fibers that contribute to anti-inflammatory, antioxidant, and lipid-lowering effects, thereby supporting metabolic health and weight regulation [7,8].

Watermelon rind powder (WRP), derived from the outer layers of *Citrullus lanatus* of the *Cucurbitaceae* family, represents a sustainable, functional food ingredient with promising therapeutic benefits. Egypt is a major producer of watermelon, generating over 2 million metric tons annually [9]. The rind, which constitutes approximately 30% of the fruit, is often discarded despite its nutritional richness. It contains high levels of dietary fiber (14.5%), protein (19.1%), and minor fat (1.22%), along with bioactive compounds such as citrulline and flavonoids like coumaric acid [10,11,12]. These constituents have been shown to exhibit antioxidant, anti-inflammatory, and antihypertensive effects, which are crucial in preventing and managing obesity and its related metabolic complications [13,14]. The fiber content also contributes to satiety and improved glucose regulation, supporting its role in functional food applications aimed at weight control and metabolic health.

Similarly, date seed powder (DSP), obtained from *Phoenix dactylifera* L. of the *Arecaceae* family, is another byproduct with high nutritional and therapeutic value. Egypt, being the leading global producer of dates, generates large quantities of seeds annually—up to 15% of the fruit's total weight [8,9]. These seeds are rich in fiber (10–13%), healthy fats (notably oleic and lauric acids), protein (5–7%), and a wide range of minerals such as potassium and magnesium [14]. Phytochemically, they are abundant in polyphenols, flavonoids, and phenolic acids, including gallic, ferulic, and caffeic acids, which impart potent antioxidant and anti-inflammatory properties [15,16]. Recent animal studies have shown that DSP supplementation can modulate lipid profiles, enhance liver function, and mitigate metabolic alterations associated with high-fat diets reinforcing its potential as a nutraceutical intervention for obesity [17].

Taken together, both watermelon rind and date seed powders offer a compelling case for inclusion in dietary strategies aimed at managing obesity and its complications, particularly in economically constrained regions where conventional pharmacotherapies may be inaccessible or unsuitable. Their nutritional density, therapeutic bioactivity, and sustainability as food industry byproducts make them ideal candidates for further investigation. Therefore, the purpose of this study is to evaluate the potential effects of watermelon rind and date seed powders on obesity-related complications in rats induced by a high-fat diet, with the broader goal of exploring these natural agents as alternative interventions for obesity management.

2. Materials and Methods

2.1. Materials

2.1.1. Plant Materials

Fresh watermelon (*Citrullus lanatus*) fruits were procured from local markets in Shebin El-Kom City, affiliated with Menoufia University, Egypt. Seeds of

Khalas date (*Phoenix dactylifera* L.) were obtained through a special arrangement with local date processing facilities in Siwa Oasis, Matrouh Governorate, Egypt. The identity and authenticity of the date seed samples were confirmed by specialists from the Faculty of Agriculture, Menoufia University, Shebin El-Kom, Egypt.

2.1.2. Chemicals and Kits

The chemicals reduced glutathione (GSH) and Ellman's reagent (5,5'-dithiobis-(2-nitrobenzoic acid), or DTNB) were procured from *Sigma Chemical Co.* (St. Louis, MO, USA). Casein was supplied by Morgan Chemical Co. in Cairo, Egypt. Other necessary materials, including food-grade vitamins, salts, and analytical-grade solvents, were obtained from El-Ghomhorya Company for Trading Drugs, *Chemicals, and Medical Instruments*, also located in Cairo. Biochemical assay kits were sourced from multiple suppliers: ALT, AST, ALP, TP, Alb, Glb, GGT, uric acid, creatinine, and glucose kits were obtained from BIODIAGNOSTIC (Dokki, Giza, Egy.); antioxidant markers like SOD and GSH from Creative BioLab (New York, USA); and lipid profile kits (TG, TC, HDL-C, LDL-C) from El-Nasr Pharmaceutical Chemicals (Cairo, Egy.).

2.2. Methods

2.2.1. Watermelon Rind Powder (WRP)

Following methods described by El-Qabari [18] and Elhassaneen et al., [19], watermelon rind (white and green outer layers, see Figure 1) was separated from the pulp, chopped using a chipping machine, and dried in a hot-air oven in two stages: 60°C for 6 hours followed by 40°C for another 6 hours, aiming for a final moisture content of approximately 10%. The dried material was milled and sieved through an 80-mesh screen. The powder was stored in polyethylene bags at 4°C until further use.

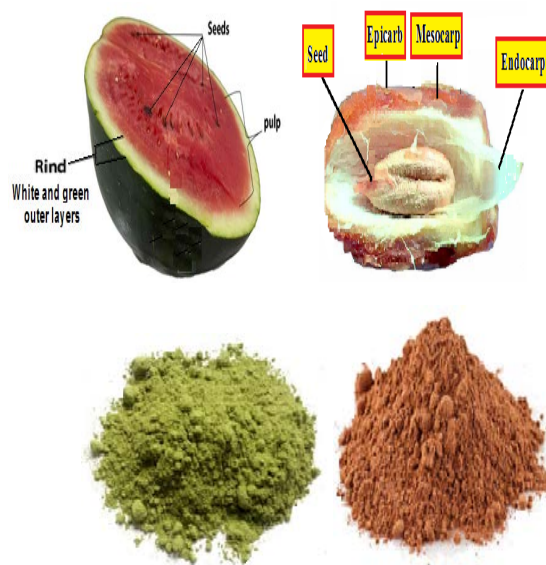


Figure 1. Powders of watermelon rind (WRP) and date seeds (DSP) were used in the study

2.2.2. Date Seed Powder (DSP)

According to Ismail et al., [20], Khalas date seeds (See Figure 1) were manually sorted, washed to remove impurities, and oven-dried at 70°C for 3 hours using a forced-air oven. The dried seeds were finely ground with a high-speed grinder (Moulinex, ElAraby Co., Benha, Egypt), sieved through a 40-mesh, and stored in airtight polyethylene bags at 4°C for experimental use.

2.2.3. Biological Experiment

2.2.3.1. Ethical Compliance

All experimental protocols were approved by the Scientific Research Ethics Committee at the Faculty of Home Economics, Menoufia University (Approval # 29-SREC-06-2023).

2.2.3.2. Animals

Adult male albino rats, weighing an average of 155.83 ± 5.72 grams each, were sourced from the Helwan Station, which belongs to the Ministry of Health and Population in Helwan, Cairo, Egy.

2.2.3.3. Standard/Basal Diet (BD)

The basal diet provided to the animals was prepared according to the formulation outlined by Reeves and colleagues in 1993. This diet comprised 10% protein, 10% corn oil, a 1% vitamin mixture, 4% mineral mixture, 0.2% choline chloride, 0.3% methionine, and 5% cellulose. The remaining 69.5% of the diet consisted of corn starch. The vitamin and mineral mixtures were prepared according to the guidelines provided by Reeves et al., [21].

2.2.3.4. High-Fat Diet (HFD)

The high-fat diet used in this study comprised 45% fat (from sheep fat and butter), 35% carbohydrates (from sucrose and starch), and 20% protein (casein). After 8 weeks of HFD consumption, the rats exhibited significant obesity, insulin resistance, and liver dysfunction, including fatty liver [22].

2.2.3.5. Experimental Design

The experimental protocol adhered to the ethical standards outlined by the Institute for Laboratory Animal Resources [23]. A total of 36 adult male rats were individually housed in wire-mesh cages under controlled environmental conditions: temperature (25 ± 3°C), relative humidity (55 ± 2%), and a 12-hour light/dark photoperiod. Prior to the commencement of the study, all animals underwent a one-week acclimatization period during which they were provided with a standard basal diet (BD). Following acclimatization, the animals were randomly allocated into two main groups. Group 1, comprising six rats, served as the normal control and continued on the BD throughout the study. The remaining 30 rats were assigned to Group 2 and subjected to obesity induction by being fed a high-fat diet (HFD) for eight consecutive weeks. After the induction phase, Group 2 was divided into five subgroups for dietary intervention: the model control group continued on the BD as a positive control (obese rats), while Groups 3 and 4 were administered BD supplemented with 5% and 10% watermelon rind powder

(WRP), respectively. Similarly, Groups 5 and 6 received BD enriched with 5% and 10% date seed powder (DSP), respectively. The inclusion levels of WRP and DSP were selected based on prior research [24,25]. Throughout the 10-week intervention period, all rats remained in individual cages. Body weights were recorded at baseline, monitored weekly, and documented at the end of the experimental duration.

2.2.3.6. Biological Evaluation

Throughout the 10-week experimental period, the daily food consumption of the rats was documented, and their body weight was measured weekly. To assess growth and feeding efficiency, body weight gain (BWG, %), feed intake (FI), and the feed efficiency ratio (FER) were calculated based on the methods described by Chapman et al., [26] by equations:

$$\text{BWG}(\%) = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

$$\text{FER} = \frac{\text{Grams gain in body weight (g / 56day)}}{\text{Grams feed intake (g / 56day)}}$$

2.2.3.7. Blood Collection and Serum Preparation

At the conclusion of the 10-week study period, blood samples were obtained following an overnight fasting period of approximately 12 hours. To ensure minimal discomfort, the rats were anesthetized with ether prior to blood collection via the abdominal aorta. Collected blood was transferred into sterile, dry centrifuge tubes and left undisturbed at room temperature to allow for clot formation. The samples were then centrifuged at 3000 revolutions per minute for 10 minutes to facilitate serum separation, following the method described by Drury and Wallington, [27]. The resulting serum was carefully transferred into labeled tubes and stored at -20°C until required for biochemical analysis.

2.2.3.8. Organ Collection and Processing

Following the sacrifice of the animals, the liver, kidneys, and heart were promptly excised. Any residual blood was gently removed by rinsing the organs with cold saline solution. The cleaned tissues were then blotted dry using sterile filter paper, weighed precisely, and preserved in 10% neutral-buffered formalin for histopathological assessment, as described by Drury and Wallington, [27]. For biochemical evaluations, liver homogenates were prepared following the procedure outlined by El-Khawaga et al., [28]. In brief, a known weight of liver tissue was homogenized in ice-cold 0.9% saline using a Teflon homogenizer. The homogenate was adjusted to a final concentration of 5% (w/v) and centrifuged at 5000 rpm for 30 minutes at 4°C. The supernatant obtained was collected and stored for subsequent biochemical analyses.

2.2.3.9. Biochemical Analyses

a. Liver function

Liver functions were determined using specific methods as: alkaline Phosphatases (ALP) pointed out by Belfield et al., [29], aspartate aminotransferase (AST), alanine aminotransferase (ALT) according to Henry et al., [30], Gamma-Glutamyl Trans peptidase (GGT), according to

Young et al., [31], total Bilirubin (T.B) according to Drut and Glick, [32], direct Bilirubin (D.B) according to Bergmeyer and Harder [33], and indirect bilirubin (ID. B) according to Kachmar and Moss [34].

b. Glucose, insulin and leptin

Serum glucose was measured using the colorimetric method of Tietz [35]. Insulin was quantified following the colorimetric detection method described by Mirsalari and Elhami [36], and leptin levels were measured using the colorimetric technique of Guntupalli and Wilson, [37].

c. Kidney function

Serum levels of urea, creatinine, and uric acid were measured using the methods outlined by Malhotra, [38], Henry et al., [30] and Schultz and Kasten, [39], respectively.

d. Immunological functions

Serum total Protein (T.P), albumin (Alb) and globulin (G), were determined consistent by Varley et al., [40], Reinhold, [41], and Reinhold et al., [42].

e. Lipids Profile

Triglycerides (TGs), total cholesterol (TC), HDL-cholesterol, and LDL-cholesterol levels in serum were determined using methods by Ahmadi et al., [43], Fossati and Prencipe, [44], Lopes-Virella et al., [45], and Richmond, [46], respectively.

f. Antioxidant status

Hepatic antioxidants, including reduced glutathione (GSH), glutathione peroxidase (GSH-Px) and catalase (CAT), were measured as per the methods of Owens and Belcher, [47], Splittgerber and Tappel, [48] and Aebi, [49], correspondingly. Superoxide dismutase (SOD) activity was assessed using a colorimetric assay kit (Creative BioLab, NY) following the method of Marklund, and Marklund, [50].

2.2.3.10. Histological Tissue Preparation

Liver and heart tissues samples from all experimental groups were fixed in 10% neutral-buffered formalin. The tissues were dehydrated through increasing ethanol concentrations (70%, 80%, and 90%), cleared in xylene, and embedded in paraffin. Thin sections (4-6 μ m) were prepared and stained with Hematoxylin and Eosin, following the methods of Bancroft and Gamble, [51].

2.4. Statistical Analysis

All measurements were performed in triplicate, and the results are presented as the mean along with the standard deviation (SD). Statistical analysis of the data was conducted using Student's t-test and MINITAB 12 software (Minitab Inc., State College, PA). To determine substantial variations between the experimental groups, a one-way ANOVA was employed, followed by Duncan's multiple comparison test. Statistical significance was defined as a p-value of 0.05 or less ($p \leq 0.05$).

3. Results and Discussion

3.1. Impact of a 10-week Treatment with Watermelon rind (WRP) and Date Seed (DSP) Powders on Body Weight Gain (BWG), Feed Efficiency Ratio (FER) and Feed intake (FI) of Obese Rats

Data in Table 1 presents the effects of a 10-week treatment with watermelon rind powder (WRP) and date seed powder (DSP) on body weight gain (BWG), feed intake (FI), and feed efficiency ratio (FER) in obese rats induced by a high-fat diet (HFD). The results are expressed as means $\pm$ standard deviation (SD), along with percentage changes relative to the normal and model control groups. For BWG, the normal control group (G1) showed a moderate body weight gain (BWG) of $0.97 \pm 0.05\%$, which is typical for healthy rats over a 10-week period. In comparison, the model controls (G2), composed of obese rats induced by a high-fat diet, exhibited a significant increase in BWG ($1.51 \pm 0.11\%$), representing a 55.67% higher BWG in comparison with the normal control, verifying the success of the high-fat diet in inducing obesity and the typical hyperphagic response observed in obese animals. Treatment with watermelon rind powder (WRP) led to a dose-dependent reduction in body weight gain in the WRP groups (G3 and G4): G3 (WRP, 5%) showed a 16.55% reduction in BWG ($1.26 \pm 0.03\%$), while G4 (WRP, 10%) demonstrated a 31.12% reduction in BWG ($1.04 \pm 0.09\%$), suggesting that higher doses of WRP are more effective at reducing BWG in obese rats. On the other hand, treatment with date seed powder (DSP) also reduced BWG but to a lesser extent: G5 (DSP, 5%) showed a 12.58% reduction in BWG ($1.32 \pm 0.05\%$), and G6 (DSP, 10%) exhibited a 24.50% reduction in BWG ($1.14 \pm 0.02\%$), indicating that DSP may have a weaker but still effective impact on reducing BWG compared to WRP. For FI, the normal control group (G1) had an average feed intake (FI) of 12.56 ± 0.66 g/day/rat, while the model control group (G2), consisting of obese rats, showed a significant increase in FI to 17.41 ± 0.57 g/day/rat, which represents a 38.61% increase compared to the normal group, reflecting the hyperphagic behavior typical in obese animals [52]. Both WRP and DSP treatments resulted in a reduction in feed intake in a dose-dependent manner. In the WRP groups, G3 (WRP, 5%) showed a 13.44% decrease in FI (15.07 ± 0.09 g/day/rat), and G4 (WRP, 10%) exhibited a 20.10% decrease in FI (13.91 ± 0.21 g/day/rat), suggesting that WRP may contribute to appetite suppression. Similarly, the DSP groups also showed reductions in FI: G5 (DSP, 5%) had an 11.25% decrease in FI (15.45 ± 1.01 g/day/rat), and G6 (DSP, 10%) had a 19.70% decrease in FI (13.98 ± 0.60 g/day/rat). This might be ascribed to the appetite-regulating effects of the compounds bioactive in both watermelon peel and date seeds, such as fibers and polyphenols [53]. For FER, the normal control group (G1) had a feed efficiency ratio (FER) of 0.082 ± 0.009 g, reflecting the efficient conversion of feed into body mass.

In comparison, the model controls (G2), composed of obese rats, exhibited an increased FER of 0.095 ± 0.010 g, indicating less efficient feed utilization. Both WRP and DSP treatments resulted in a reduction in FER, suggesting improved feed efficiency. In the WRP groups, G3 (WRP, 5%) showed an 8.42% reduction in FER (0.087 ± 0.005 g), and G4 (WRP, 10%) exhibited an 11.57% reduction in FER (0.084 ± 0.004 g). Similarly, the DSP groups demonstrated improved feed efficiency, with G5 (DSP, 5%) showing a 6.31% reduction in FER (0.089 ± 0.009 g) and G6 (DSP, 10%) showing a 10.52% reduction in FER (0.085 ± 0.005 g). These reductions in FER in both WRP and DSP groups suggest that these treatments may help improve metabolic efficiency by promoting better fat oxidation or reducing fat deposition, as noted by El-Sayed et al., [54].

The results from this study are in line with earlier studies that examined the anti-obesity effects of watermelon peel and date seed powders. For instance, several previous studies reported similar reductions in body weight gain and feed intake in animals treated with plant-based powders [55,56,57,58,59,60,61]. Watermelon rind, which contains polyphenols and fiber, has been registered to possess antioxidant, anti-inflammatory, and weight-reducing properties. As, a study by Huseini, and Ghaffari, [61] demonstrated that date seed powder significantly reduced body weight and improved insulin sensitivity in high-fat diet-induced obese rats. The current study's findings of reduced BWG and FI in DSP-treated groups are consistent with these results. Furthermore, studies on feed efficiency also suggest that plant-derived fibers and bioactive compounds can improve the utilization of dietary fat, as observed in the reduction of FER in treated rats [62,63,64,65,66,67].

The observed lower body weight gain (BWG), feed intake (FI), and feed efficiency ratio (FER) in the groups

treated with watermelon rind powder (WRP) and date seed powder (DSP) can be attributed to multiple factors, including appetite suppression, enhanced fat metabolism, and their rich antioxidant content. Both WRP and DSP are known to contain bioactive compounds that may help regulate appetite through mechanisms such as increased satiety [68]. The dietary fibers and polyphenols found in these powders can promote the release of satiety hormones like leptin and insulin. These treatments may also improve lipid metabolism and boost fat oxidation, which may explain the reduction in BWG and FER. Previous studies have demonstrated that plant-derived compounds found in WRP and DSP can support lipolysis and inhibit adipogenesis [69]. Additionally, watermelon peel and date seeds are rich in antioxidants, which can help reduce oxidative stress and inflammation—both of which are commonly elevated in obesity [59]. Research indicates that the potential benefits of certain plant components in managing obesity may stem from their rich composition of diverse phytochemicals. These include substances like alkaloids, phenolic acids, anthocyanins, carotenoids, flavonols, organosulfur compounds, and phytosterols [70,71,72]. These groups of phytochemicals have demonstrated the ability to modulate gene expression and cellular processes, particularly within fat cells (adipocytes), through various pathways. Their mechanisms of action involve interacting with nuclear receptor transcription factors, altering the activity of other transcription factors, regulating signaling pathways linked to inflammation and oxidative stress, and engaging in non-genomic activities such as neutralizing reactive oxygen species [56,73,74,75]. Collectively, these actions contribute to their capacity to influence adipocyte function, fat accumulation, and overall obesity.

Table 1. Impact of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on body weight gain (BWG), feed efficiency ratio (FER) and feed intake (FI) of obese rats

Groups	BWG (%)		FI (g/day/rat)		FER(g)	
	Means $\pm$ SD	% of change	Means $\pm$ SD	% of change	Means $\pm$ SD	% of change
G1: Normal control	$0.97^d \pm 0.05$	0.00	$12.56^d \pm 0.66$	0.00	$0.082^b \pm 0.009$	0.00
G2: Model control	$1.51^a \pm 0.11$	55.67	$17.41^a \pm 0.57$	38.61	$0.095^a \pm 0.010$	15.85
G3 (WRP, 5%)	$1.26^b \pm 0.03$	-16.55	$15.07^{ab} \pm 0.09$	-13.44	$0.087^b \pm 0.005$	-8.42
G4 (WRP, 10%)	$1.04^{cd} \pm 0.09$	-31.12	$13.91^c \pm 0.21$	-20.10	$0.084^b \pm 0.004$	-11.57
G5 (DSP, 5%)	$1.32^{ab} \pm 0.05$	-12.58	$15.45^b \pm 1.01$	-11.25	$0.089^{ab} \pm 0.009$	-6.31
G6 (DSP, 10%)	$1.14^c \pm 0.02$	-24.50	$13.98^c \pm 0.60$	-19.70	$0.085^b \pm 0.005$	-10.52

The results are expressed as means $\pm$ SD (n=6). Statistical significance is indicated by different superscript letters within the same column ($P \leq 0.05$). Values in parentheses represent the percentage of change (%), with comparisons made between the obese (Model) group and the normal group, as well as between the groups treated with plant parts (WRP and DSP) and the obese group. G1 (Normal control) represents healthy rats without treatment; G2 (Model control) includes obese rats induced by a high-fat diet (HFD) with no treatment; WRP and DSP refer to watermelon rind powder and date seed powder, respectively. G3, G4, G5, and G6 are the obese groups treated with WRP and DSP at 5 and 10 g/100g diet concentrations for 8 weeks. "bw" stands for body weight.

3.2. Influence of a 10-week Treatment with Watermelon Rind (WRP) and Date Seed (DSP) Powders on Some Organs Weight in Obese Rat

Table 2 presents the influence of a 10-week treatment with watermelon rind powder (WRP) and date seed powder (DSP) on the weight of the liver, kidney, and heart in obese rats, which are crucial indicators of physiological changes reflecting alterations in metabolism, tissue growth,

and function, particularly in the context of obesity and related disorders. The model control group (G2), induced with obesity through a high-fat diet, showed increases in liver weight (14.73%), kidney weight (10.59%), and heart weight (8.52%), consistent with previous studies reporting organ hypertrophy in obesity, particularly in the liver and heart (59,76,77). The increase in liver weight likely reflects hepatic steatosis, where fat accumulates in the liver due to disturbed lipid metabolism, while the increase in heart weight may indicate cardiac hypertrophy, often associated with the added workload on the heart in obesity.

Kidney enlargement is also a known consequence of obesity-related kidney disease, often leading to hyperfiltration and increased renal workload [78]. Treatment with WRP demonstrated a dose-dependent effect on organ weights. In the 5% WRP group (G3), slight reductions in liver weight (-5.03%), kidney weight (-3.89%), and heart weight (-4.95%) were observed, indicating that WRP may have a protective or normalizing effect on organ hypertrophy caused by obesity, likely due to its antioxidant and anti-inflammatory properties. Watermelon peel is known for its polyphenols, which possess antioxidant and anti-inflammatory effects that could decrease oxidative stress and inflammation in various organs, thus alleviating the hypertrophy commonly seen in obesity (58). In the 10% WRP group (G4), liver weight decreased significantly by -12.09%, kidney weight by -6.58%, and heart weight by -17.76%, suggesting that higher doses of WRP may be more effective in counteracting obesity-induced organ hypertrophy. The higher concentration of bioactive compounds such as flavonoids and polyphenols in the 10% WRP group likely contributed to a more pronounced improvement in organ weights [79]. DSP also showed positive effects on organ weights, though the changes were less pronounced than with WRP. In the 5% DSP group (G5), liver weight decreased by -3.77%, kidney weight by -2.99%, and heart weight by -6.81%, indicating that DSP may have protective effects against obesity-induced organ enlargement, though to a lesser degree. The bioactive compounds in DSP, including polyphenols and flavonoids, are known for their antioxidant and anti-

inflammatory properties, which may help reduce oxidative stress and inflammation in the liver, kidney, and heart, improving organ weights in obese rats [80,81]. In the 10% DSP group (G6), liver weight decreased by -2.77%, kidney weight by -4.79%, and heart weight by -16.73%, suggesting that while DSP has beneficial effects on organ weights, its efficacy may be lower than WRP, possibly due to differences in the composition and bioavailability of bioactive compounds in the two treatments.

The study results align with similar on the effects of natural plant powders on obesity-induced organ hypertrophy. Studies on watermelon rind powder have demonstrated its antioxidant and anti-inflammatory properties, which aid in lowering oxidative stress and inflammation, thus preventing obesity-related organ damage [19,79,82]. The reductions in organ weight observed with WRP in the same study are in comparison with those seen in other studies examining the effects of polyphenolic-rich extracts on obesity-induced hypertrophy [58]. Similarly, studies on date seed powder also report beneficial effects on oxidative stress and organ weight in obese models [75,80]. However, compared to WRP, DSP's effects are less pronounced, which may be attributed to the differences in the types and concentrations of antioxidants present in watermelon peel and date seed. In line of Zhao et al., [59], higher doses of WRP tend to have more significant protective effects, likely due to the greater availability of bioactive compounds that can mitigate oxidative damage in the liver, kidney, and heart.

Table 2. Influence of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on some organs weight in obese rat

Groups	Liver (g)		Kidney (g)		Heart (g)	
	Means $\pm$ SD	% of change	Means $\pm$ SD	% of change	Means $\pm$ SD	% of change
G1: Normal control	3.46 $^{\pm}$ 0.565	0.00	3.02 $^{\pm}$ 0.22	0.00	4.46 $^{\pm}$ 1.939	0.00
G2: Model control	3.97 $^{\pm}$ 0.592	14.73	3.34 $^{\pm}$ 0.20	10.59	4.84 $^{\pm}$ 0.037	8.52
G3 (WRP, 5%)	3.77 $^{\pm}$ 0.256	-5.03	3.21 ab $\pm$ 0.23	-3.89	4.60 ab $\pm$ 0.639	-4.95
G4 (WRP, 10%)	3.49 $^{\pm}$ 0.429	-12.09	3.12 $^{\pm}$ 0.13	-6.58	3.98 $^{\pm}$ 0.166	-17.76
G5 (DSP, 5%)	3.82 ab $\pm$ 0.474	-3.77	3.24 $^{\pm}$ 0.11	-2.99	4.51 $^{\pm}$ 0.047	-6.81
G6 (DSP, 10%)	3.86 $^{\pm}$ 0.63	-2.77	3.18 bc $\pm$ 0.02	-4.79	4.03 $^{\pm}$ 0.230	-16.73

The results are expressed as means $\pm$ SD (n=6). Statistical significance is indicated by different superscript letters within the same column ($P \leq 0.05$). Values in parentheses represent the percentage of change (%), with comparisons made between the obese (Model) group and the normal group, as well as between the groups treated with plant parts (WRP and DSP) and the obese group. G1 (Normal control) represents healthy rats without treatment; G2 (Model control) includes obese rats induced by a high-fat diet (HFD) with no treatment; WRP and DSP refer to watermelon rind powder and date seed powder, respectively. G3, G4, G5, and G6 are the obese groups treated with WRP and DSP at 5 and 10 g/100g diet concentrations for 8 weeks. "bw" stands for body weight.

3.3. Impact of a 10-week Treatment with Watermelon rind (WRP) and Date Seed (DSP) Powders on the Liver Function of Obese Rats

Data in Table 3 presents the effects of watermelon rind powder (WRP) and date seed powder (DSP) on liver function in obese rats, measured by serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), which are key markers of liver damage. In the model controls (G2), which got no therapy, liver enzyme levels were significantly elevated in comparison with the normal controls (G1), with ALT increasing by 99.02%, AST by 58.63%, and ALP by 188.91%. These increases indicate liver damage, consistent with other studies that link

elevated liver enzymes to obesity-induced metabolic stress (83; 84; 64; 59; 85 and 86; 87 and 88). In the WRP-treated groups, a dose-dependent reduction in liver enzyme levels was observed, with the 5% WRP treatment (G3) reducing ALT by 30.03%, AST by 20.21%, and ALP by 36.08%, while the 10% WRP treatment (G4) resulted in reductions of 40.39% for ALT, 40.58% for AST, and 37.55% for ALP. These reductions suggest that WRP has a hepatoprotective effect, likely due to its high antioxidant content, including flavonoids and polyphenols, which are known to reduce oxidative stress and inflammation in the liver [19,58,71,82]. Regarding DSP, the 5% treatment (G5) led to a decrease in ALT by 33.14%, AST by 6.92%, and ALP by 30.29%, while the 10% DSP treatment (G6) resulted in a smaller decrease in ALT (15.97%) but a significant reduction in AST (41.25%) and ALP (21.24%). Although DSP showed a lower efficacy than WRP,

possibly due to its different bioactive profile, including polyphenols and dietary fibers, it still demonstrated protective effects against liver dysfunction, especially at higher doses [59,89]. These findings suggest that both WRP and DSP may have potential as natural interventions for obesity-related liver damage, with WRP showing more pronounced effects.

Several studies have explored the hepatoprotective effects of plant-based compounds, particularly those derived from watermelon peel and date seeds, which are rich in antioxidants, polyphenols, and other bioactive compounds. The results of the present study align with these studies, as both WRP and DSP demonstrate the potential to reduce liver enzyme activities and improve liver function in obese rats. The reductions in liver enzymes observed with WRP treatment are consistent with previous findings. For example, Abdel-Hamid et al., [90] reported that watermelon peel extract significantly reduced ALT and AST levels in rats with diet-induced obesity, likely due to the high levels of polyphenolic compounds with antioxidant properties. Similarly, Mahran et al., [72] found that watermelon peel extract alleviated oxidative stress and liver damage in obese rats, which supports the current findings of the present study. DSP also showed significant improvements in liver enzyme levels, although the effects were less pronounced compared to WRP. Studies by Zhao et al., [59] have demonstrated the antioxidant properties of date seeds, which may help reduce liver inflammation and oxidative damage. However, the results from Table 3 suggest that DSP's effectiveness may depend on the dose, with higher concentrations yielding more significant reductions in liver enzyme activities. This is similar to El-Sayed et al., [69] who reported that date seed extracts reduced liver enzyme levels in rats with induced liver damage.

The hepatoprotective effects seen with both watermelon rind powder (WRP) and date seed powder (DSP) can likely be attributed to the presence of compounds bioactive in these plant materials. Watermelon peel is abundant in flavonoids, carotenoids, and polyphenolic acids, all of which are well-known for their strong antioxidant and anti-inflammatory properties [71]. These compounds likely help reduce oxidative stress and inflammation in the liver, leading to an improvement in liver function. Date seed powder, although also rich in antioxidants and dietary fiber, may exert its protective impacts through distinct mechanisms, such as influencing lipid metabolism and decreasing fat accumulation in the liver [59]. Moreover, previous research has suggested that other plant parts, rich in polyphenolic compounds like WRP and DSP, can lower liver enzyme levels by various mechanisms, including inhibiting the hepatocellular uptake of bile acids, enhancing the liver's antioxidant capacity, reducing bilirubin levels, protecting hepatocytes from damage, and scavenging reactive oxygen species (ROS) [56,57,58,89,91,92,93,94,95,96,97]. Furthermore, both WRP and DSP may modulate signaling pathways related to oxidative stress and inflammation, as indicated by their influence on gene expression and enzyme activity. The observed reductions in ALT and AST levels suggest less hepatocellular injury, while the decrease in ALP may point to enhanced liver function and reduced inflammation of the bile ducts [58].

3.4. Influence of a 10-week Treatment with Watermelon Rind (WRP) and Date Seed (DSP) Powders on Liver Function Markers (total protein, TP, albumin, Alb, globulin, Glb, Alb/Glb ratio, and gamma-glutamyl transferase, GGT) in Obese Rats

Table 4 summarizes the results of a 10-week treatment with watermelon rind powder (WRP) and date seed powder (DSP) on various liver function markers, including total protein (TP), albumin (Alb), globulin (Glb), albumin/globulin ratio (A/G), and gamma-glutamyl transferase (GGT) in obese rats. These markers are essential for evaluating liver health, and alterations in their levels typically indicate liver dysfunction. The model control group (G2), representing obese rats induced by a high-fat diet, exhibited significant reductions in TP, Alb, and Glb by 33.23%, 37.05%, and 28.10%, respectively, alongside a decrease in the A/G ratio by 11.71% and a dramatic increase in GGT by 568.62%. These changes indicate significant liver damage, consistent with studies linking high-fat diets to liver dysfunction and oxidative stress [56,59,69] [77,99,100]. Treatment with WRP resulted in improvements in liver function markers, particularly in the 10% WRP group (G4), where TP, Alb, and Glb increased by 41.45%, 49.19%, and 32.27%, respectively, and the A/G ratio improved by 12.38%. Additionally, GGT levels decreased by 78.95%, suggesting a hepatoprotective effect of WRP, possibly due to its antioxidant-rich polyphenols, flavonoids, and carotenoids [58;71]. In the 5% WRP group (G3), TP, Alb, and Glb showed smaller improvements, and the A/G ratio decreased slightly by 5.30%. DSP treatment also showed hepatoprotective effects, with more modest improvements compared to WRP. In the 5% DSP group (G5), TP, Alb, and Glb increased by 52.35%, 63.30%, and 38.63%, respectively, with the A/G ratio improving by 17.69%, and GGT decreased by 88.19%. In the 10% DSP group (G6), TP, Alb, and Glb improved by 30.34%, 35.08%, and 25.45%, respectively, with a slight improvement in the A/G ratio by 7.07%, and GGT decreased by 65.24%. These results suggest that while DSP is less potent than WRP, it still exerts protective effects, likely due to its antioxidant and anti-inflammatory properties, attributed to its polyphenols and dietary fiber [59,80]. The observed differences in efficacy between the two treatments may stem from the distinct bioactive compounds found in WRP and DSP, which contribute to their respective hepatoprotective effects.

The results obtained in same study are in line with prior research highlighting the beneficial effects of plant-derived bioactive compounds on liver health, particularly in the context of obesity-induced liver dysfunction. The hepatoprotective effects of watermelon peel have been widely reported in the literature. For instance, Hassan, [71] demonstrated that watermelon peel extract alleviates oxidative stress and inflammation in liver dysfunction. Also, El-Qabari, [82], Mahran et al., [98] and Ismail et al., [101] further confirmed that watermelon peel extract reduced liver damage and oxidative stress, leading to improved liver function. In the present study, the observed

improvements in TP, Alb, Glb, and GGT following WRP treatment further support these findings. The significant improvement in liver function markers at higher doses of WRP (10%) is consistent with the dose-dependent effects observed in previous studies on watermelon peel. Similarly, DSP has shown hepatoprotective properties in various studies. Zhao et al., [59] found that date seed polyphenols improved liver function in obesity-induced rats by reducing oxidative stress and modulating lipid metabolism. Also, Elmaadawy et al., [73] reported the

protective effects of date seed extract on liver function, including reductions in liver enzymes and improvements in serum protein levels. The present data aligns with these findings, showing significant improvements in liver function markers following DSP treatment, particularly at the 5% concentration. Although DSP exhibited protective effects, the magnitude of improvement was less pronounced compared to WRP, which might be due to the different bioactive compounds present in watermelon peel and date seeds.

Table 3. Impact of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on the liver function of obese rats

Groups	Serum alanine aminotransferase activity (ALT, U/L)		Serum Aspartate aminotransferase activity (AST, U/L)		Serum alkaline phosphatase activity (ALP, U/L)	
	Means $\pm$ SD	% of change	Means $\pm$ SD	% of change	Means $\pm$ SD	% of change
G1: Normal control	36.81 ^d $\pm$ 6.135	0.00	62.76 ^c $\pm$ 4.137	0.00	125.18 ^e $\pm$ 13.91	0.00
G2: Model control	73.26 ^a $\pm$ 5.24	99.02	99.56 ^a $\pm$ 2.09	58.63	361.66 ^a $\pm$ 13.72	188.91
G3 (WRP , 5%)	51.29 ^c $\pm$ 4.68	-30.03	79.43 ^b $\pm$ 7.77	-20.21	231.16 ^d $\pm$ 10.56	-36.08
G4 (WRP , 10%)	43.67 ^{cd} $\pm$ 6.94	-40.39	59.15 ^c $\pm$ 5.39	-40.58	225.85 ^d $\pm$ 17.32	-37.55
G5 (DSP, 5%)	48.98 ^c $\pm$ 5.27	-33.14	92.67 ^a $\pm$ 5.56	-6.92	252.11 ^c $\pm$ 9.74	-30.29
G6 (DSP, 10%)	61.56 ^b $\pm$ 4.90	-15.97	58.49 ^c $\pm$ 3.68	-41.25	284.82 ^b $\pm$ 15.43	-21.24

The results are expressed as means $\pm$ SD (n=6). Statistical significance is indicated by different superscript letters within the same column ($P \leq 0.05$). Values in parentheses represent the percentage of change (%), with comparisons made between the obese (Model) group and the normal group, as well as between the groups treated with plant parts (WRP and DSP) and the obese group. G1 (Normal control) represents healthy rats without treatment; G2 (Model control) includes obese rats induced by a high-fat diet (HFD) with no treatment; WRP and DSP refer to watermelon rind powder and date seed powder, respectively. G3, G4, G5, and G6 are the obese groups treated with WRP and DSP at 5 and 10 g/100g diet concentrations for 8 weeks. "bw" stands for body weight.

Table 4. Influence of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on liver function markers (T.P, ALB, Glb, A/G and GGT) in obese rats

Groups	T.P (mg/dL)	ALB (mg/dL)	Glb (mg/dL)	A/G (mg/dL)	GGT (mg/dL)
G1: Normal control	7.01 ^a $\pm$ 0.118 (0.00)	3.94 ^a $\pm$ 0.088 (0.00)	3.06 ^a $\pm$ 0.121 (0.00)	1.28 ^{ab} $\pm$ 0.067 (0.00)	2.04 ^{de} $\pm$ 0.320 (0.00)
G2: Model control	4.68 ^c $\pm$ 0.429 (-33.23)	2.48 ^c $\pm$ 0.088 (-37.05)	2.20 ^c $\pm$ 0.340 (-28.10)	1.13 ^c $\pm$ 0.137 (-11.71)	13.64 ^a $\pm$ 1.698 (568.62)
G3 (WRP , 5%)	5.13 ^d $\pm$ 0.309 (9.61)	2.65 ^d $\pm$ 0.140 (6.85)	2.47 ^b $\pm$ 0.206 (12.27)	1.07 ^d $\pm$ 0.053 (-5.30)	8.05 ^b $\pm$ 0.600 (-40.98)
G4 (WRP , 10%)	6.62 ^b $\pm$ 0.134 (41.45)	3.7 ^b $\pm$ 0.088 (49.19)	2.91 ^a $\pm$ 0.125 (32.27)	1.27 ^{ab} $\pm$ 0.071 (12.38)	2.87 ^d $\pm$ 0.250 (-78.95)
G5 (DSP, 5%)	7.13 ^a $\pm$ 0.127 (52.35)	4.05 ^a $\pm$ 0.056 (63.30)	3.05 ^a $\pm$ 0.170 (38.63)	1.33 ^a $\pm$ 0.092 (17.69)	1.61 ^e $\pm$ 0.203 (-88.19)
G6 (DSP, 10%)	6.10 ^c $\pm$ 0.121 (30.34)	3.35 ^c $\pm$ 0.139 (35.08)	2.76 ^a $\pm$ 0.085 (25.45)	1.21 ^{bc} $\pm$ 0.074 (7.07)	4.74 ^c $\pm$ 0.309 (-65.24)

The results are expressed as means $\pm$ SD (n=6). Statistical significance is indicated by different superscript letters within the same column ($P \leq 0.05$). Values in parentheses represent the percentage of change (%), with comparisons made between the obese (Model) group and the normal group, as well as between the groups treated with plant parts (WRP and DSP) and the obese group. G1 (Normal control) represents healthy rats without treatment; G2 (Model control) includes obese rats induced by a high-fat diet (HFD) with no treatment; WRP and DSP refer to watermelon rind powder and date seed powder, respectively. G3, G4, G5, and G6 are the obese groups treated with WRP and DSP at 5 and 10 g/100g diet concentrations for 8 weeks. "bw" stands for body weight.

The liver function improvements observed in both WRP and DSP-treated groups can likely be attributed to the antioxidant and anti-inflammatory properties of these plant materials. Watermelon peel is rich in flavonoids, carotenoids, and polyphenolic acids, all of which are recognized for their potent antioxidant properties, which may help in reducing liver oxidative stress [19,73,74,82]. Similarly, DSP is rich in polyphenols and dietary fiber, which have been shown to improve metabolic health and liver function through mechanisms such as modulating lipid metabolism and reducing hepatic fat accumulation [59]. The differences in efficacy between the two plant materials may be due to the varying levels and types of bioactive compounds in WRP and DSP.

3.5. Influence of a 10-week Treatment with Watermelon Rind (WRP) and Date Seed (DSP) Powders on Liver Function Markers (total bilirubin, TB, direct bilirubin, DB, indirect bilirubin, IDB) in Obese Rat

Table 5 presents the impact of a 10-week treatment with watermelon rind powder (WRP) and date seed powder (DSP) on liver function markers in obese rats, specifically focusing on total bilirubin (TB), direct bilirubin (DB), and indirect bilirubin (IDB) levels, which

are critical indicators of liver function as they reflect the liver's ability to process and eliminate waste products. Elevated bilirubin levels are often associated with liver dysfunction and diseases such as jaundice, cholestasis, or hepatic inflammation [102,103]. In the model controls (G2), which represents obese rats induced by a high-fat diet, there were significant increases in all three bilirubin markers: TB increased by 126.19%, DB by 70%, and IDB by 143.75%, indicating substantial liver dysfunction, likely due to oxidative stress and inflammation caused by the high-fat diet. These results are in line with prior studies reporting liver damage and elevated bilirubin levels in obese rats or those on high-fat diets [59; 104]. The elevated TB and IDB levels suggest impaired liver conjugation and clearance of bilirubin, indicating hepatobiliary stress. Treatment with WRP showed a dose-dependent effect on bilirubin levels. In the 5% WRP group (G3), there was a significant reduction in TB, DB, and IDB, with decreases of 31.57%, 23.52%, and 33.33%, respectively, while in the 10% WRP group (G4), there was a moderate decrease in TB (16.84%), DB (11.76%), and IDB (10.25%). The reduction in bilirubin levels suggests that WRP has a hepatoprotective effect, likely due to its antioxidant and anti-inflammatory properties, which could reduce liver damage and improve bilirubin processing. Watermelon peel contains polyphenolic compounds, flavonoids, and carotenoids, which are known for their antioxidant properties and have been pointed out to alleviate oxidative stress and inflammation in various liver conditions [71,82,105]. DSP also demonstrated beneficial effects on bilirubin levels, although the magnitude of change was somewhat less pronounced compared to WRP. In the 5% DSP group (G5), TB, DB, and IDB levels decreased by 43.15%, 23.52%, and 47.43%, respectively, while in the 10% DSP group (G6), there were more modest reductions in TB (10.52%) and DB (47.05%), and a minor decrease in IDB (3.07%). Despite the smaller reductions in TB and IDB compared to WRP, DSP still exhibited hepatoprotective effects. The presence of polyphenols, dietary fiber, and other bioactive compounds in DSP may contribute to its ability to alleviate oxidative stress and improve liver function [59,78,81]. The results from this study are in line with prior studies that have shown the beneficial effects of watermelon peel and date seed on liver function. For example, El-Sayed et al., [59] reported that watermelon and date seed polyphenols have hepatoprotective effects, reducing liver damage and improving liver function markers, including bilirubin levels. Similarly, El-Sayed et al., [69] demonstrated that watermelon peel extract improves liver function by reducing oxidative stress, which aligns with the findings of this study regarding the reduction in bilirubin levels after treatment with WRP. In addition, Elmaadawy et al., [55] showed that date seed extract offers protective effects against liver damage in rats, which corresponds to the improvements observed in this study after treatment with DSP. While WRP exhibited stronger effects in improving bilirubin levels compared to DSP, both treatments demonstrated significant hepatoprotective potential, likely due to their antioxidant and anti-inflammatory properties.

Table 5. Influence of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on liver function markers (TB, DB, and IDB) in obese rat

Groups	Total bilirubin (TB, mg/dL)		Direct bilirubin (DB, mg/dL)		Indirect bilirubin (IDB, mg/dL)	
	Means $\pm$ SD	% of change	Means $\pm$ SD	% of change	Means $\pm$ SD	% of change
G1: Normal control	0.42 ^d $\pm$ 0.067	0.00	0.1 ^a $\pm$ 0.018	0.00	0.32 ^c $\pm$ 0.05	0.00
G2: Model control	0.95 ^a $\pm$ 0.042	126.19	0.17 ^a $\pm$ 0.007	70.00	0.78 ^a $\pm$ 0.03	143.75
G3 (WRP, 5%)	0.65 ^c $\pm$ 0.042	-31.57	0.13 ^a $\pm$ 0.007	-23.52	0.52 ^{bc} $\pm$ 0.03	-33.33
G4 (WRP, 10%)	0.79 ^b $\pm$ 0.189	-16.84	0.15 ^a $\pm$ 0.28	-11.76	0.70 ^a ^b $\pm$ 0.27	-10.25
G5 (DSP, 5%)	0.54 ^{cd} $\pm$ 0.043	-43.15	0.13 ^a $\pm$ 0.014	-23.52	0.41 ^c $\pm$ 0.053	-47.43
G6 (DSP, 10%)	0.85 ^{ab} $\pm$ 0.143	-10.52	0.09 ^a $\pm$ 0.087	-47.05	0.756 ^a $\pm$ 0.224	-3.07

The results are expressed as means $\pm$ SD (n=6). Statistical significance is indicated by different superscript letters within the same column ($P \leq 0.05$). Values in parentheses represent the percentage of change (%), with comparisons made between the obese (Model) group and the normal group, as well as between the groups treated with plant parts (WRP and DSP) and the obese group. G1 (Normal control) represents healthy rats without treatment; G2 (Model control) includes obese rats induced by a high-fat diet (HFD) with no treatment; WRP and DSP refer to watermelon rind powder and date seed powder, respectively. G3, G4, G5, and G6 are the obese groups treated with WRP and DSP at 5 and 10 g/100g diet concentrations for 8 weeks. "bw" stands for body weight.

3.6. Influence of a 10-week Treatment with Watermelon Rind (WRP) and Date Seed (DSP) Powders on Blood Glucose, Insulin and Leptin in Obese Rat

Table 6 presents the impact of a 10-week treatment with watermelon rind powder (WRP) and date seed powder (DSP) on blood glucose, insulin, and plasma leptin levels in obese rats, focusing on the alterations in these metabolic markers, which are essential for evaluating metabolic health. These markers provide critical insights into glucose homeostasis, insulin sensitivity, and adiposity regulation, with elevated blood glucose and insulin resistance being key indicators of metabolic dysfunction and obesity. Additionally, leptin levels are associated with fat accumulation and energy regulation. In the model controls (G2), representing obese rats induced by a high-fat diet, significant changes in all three metabolic parameters were observed. Blood glucose levels increased dramatically by 279.71%, rising from 103.99 mg/dL in the normal control group (G1) to 394.87 mg/dL, which indicates severe hyperglycemia, a sign of insulin resistance and impaired glucose metabolism. Insulin levels also decreased by 93.88%, reflecting a significant disruption in insulin secretion, likely due to the failure of pancreatic β -cells to compensate for the elevated glucose levels. Plasma leptin levels were reduced by 45.77%, suggesting impaired leptin signaling or a compensatory mechanism in response to obesity, as leptin

typically increases with fat accumulation. These findings align with several previous studies which show the detrimental effects of high-fat diets on glucose homeostasis, insulin sensitivity, and leptin signaling [59,84] [102,107] [108,109] [110,111,112].

Regarding the effects of watermelon rind powder (WRP), treatment with WRP showed significant improvements in metabolic parameters in a dose-dependent manner. In the 5% WRP group (G3), blood glucose levels decreased by 30.80%, insulin levels increased by 159.67%, and leptin levels increased by 36.69%. These findings suggest that WRP may help restore glucose homeostasis and improve insulin sensitivity, likely due to its antioxidant and anti-inflammatory properties. In the 10% WRP group (G4), further significant improvements were observed: blood glucose decreased by 56.05%, insulin levels increased by 1085.48%, and leptin levels increased by 47.24%. These improvements can be attributed to polyphenolic compounds, flavonoids, and carotenoids in watermelon peel, which have been reported to enhance insulin sensitivity, reduce oxidative stress, and promote energy balance [58,79]. For date seed powder (DSP), although the changes were less pronounced compared to WRP, DSP still demonstrated beneficial effects on metabolic markers. In the 5% DSP group (G5), blood glucose levels decreased by 66.58%, insulin levels increased by 1414.51%, and leptin levels increased by 31.65%, indicating DSP's protective effects on glucose metabolism, likely due to its antioxidant properties and ability to modulate insulin sensitivity. In the 10% DSP group (G6), blood glucose decreased by 42.76%, insulin levels increased by 598.38%,

and leptin levels increased by 41.74%. These results support previous studies by Elmaadawy et al., [55] and Zhao et al., [59], which highlight the beneficial effects of date seed extract on glucose metabolism and insulin sensitivity, likely due to its rich content of polyphenols, dietary fiber, and other bioactive compounds.

The observed improvements in blood glucose, insulin, and leptin levels following treatment with WRP and DSP are consistent with several studies on the benefits of natural products for managing obesity and metabolic disorders. Previous research has demonstrated that watermelon peel and date seed extracts contain polyphenols, flavonoids, and other bioactive compounds with antioxidant, anti-inflammatory, and insulin-sensitizing properties [58,79]. In line with the present study, previous studies have shown that watermelon peel extract improves insulin sensitivity and reduces blood glucose in animal models of obesity [59,98]. The polyphenolic compounds in watermelon peel are believed to reduce oxidative stress and inflammation, which are central contributors to insulin resistance [110,113] [114,115,116]. Similarly, date seed extract has been reported to lower blood glucose and enhance insulin sensitivity in diabetic rats, possibly through its polyphenol content and ability to regulate glucose metabolism [78]. The improvement in leptin levels following treatment with both WRP and DSP aligns with findings from other studies suggesting that polyphenol-rich extracts can improve leptin sensitivity. Leptin resistance is commonly observed in obesity, and natural antioxidants like those found in watermelon peel and date seeds have been shown to restore leptin signaling and help manage body weight and adiposity [73,78].

Table 6. Influence of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on blood glucose, insulin and leptin in obese rat

Groups	Blood glucose (mg/dl)		Insulin (µU/ml)		Plasma leptin level (ng/ml)	
	Means ±SD	% of change	Means ±SD	% of change	Means ±SD	% of change
G1: Normal control	103.99 ^b ±10.584	0.00	10.14 ^a ±0.753	0.00	4.02 ^a ±0.08	0.00
G2: Model control	394.87 ^a ±41.923	279.71	0.62 ^f ±0.209	-93.88	2.18 ^c ±0.04	-45.77
G3 (WRP , 5%)	273.23 ^b ±15.678	-30.80	1.61 ^e ±0.321	159.67	2.98 ^b ±0.21	36.69
G4 (WRP , 10%)	173.53 ^d ±8.141	-56.05	7.35 ^c ±0.527	1085.48	3.21 ^{ab} ±0.05	47.24
G5 (DSP, 5%)	131.93 ^c ±6.871	-66.58	9.39 ^b ±0.463	1414.51	2.87 ^b ±0.11	31.65
G6 (DSP, 10%)	226 ^c ±7.449	-42.76	4.33 ^d ±0.371	598.38	3.09 ^b ±0.07	41.74

The results are expressed as means ± SD (n=6). Statistical significance is indicated by different superscript letters within the same column ($P \leq 0.05$). Values in parentheses represent the percentage of change (%), with comparisons made between the obese (Model) group and the normal group, as well as between the groups treated with plant parts (WRP and DSP) and the obese group. G1 (Normal control) represents healthy rats without treatment; G2 (Model control) includes obese rats induced by a high-fat diet (HFD) with no treatment; WRP and DSP refer to watermelon rind powder and date seed powder, respectively. G3, G4, G5, and G6 are the obese groups treated with WRP and DSP at 5 and 10 g/100g diet concentrations for 8 weeks. "bw" stands for body weight.

The significant reduction in blood glucose and the substantial improvement in insulin sensitivity observed with WRP and DSP may be attributed to their potent antioxidant and anti-inflammatory effects. Both watermelon peel and date seed are rich in polyphenols, flavonoids, and other bioactive compounds that combat oxidative stress, a major contributor to insulin resistance in obesity [19,59,82]. Additionally, these compounds may help improve insulin signaling, leading to better glucose uptake and metabolism in peripheral tissues. The observed increase in leptin levels suggests a potential restoration of leptin sensitivity, which is often impaired in obesity. Leptin resistance is commonly seen in obese individuals,

where elevated leptin levels fail to suppress appetite or reduce adiposity. The bioactive compounds in WRP and DSP may help modulate leptin sensitivity, thus contributing to better energy regulation and reduced fat accumulation [58].

3.7. Impact of a 10-week Treatment with Watermelon Rind (WRP) and Date Seed (DSP) Powders on Serum Lipid Profile of Obese Rats

Table 7 evaluates the impact of a 10-week treatment

with watermelon rind powder (WRP) and date seed powder (DSP) on the serum lipid profile of obese rats, focusing on total cholesterol (T.C), triglycerides (T.G), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels, all of which are critical indicators of cardiovascular health and metabolic dysfunction, particularly in the context of obesity. Dyslipidemia, characterized by elevated T.C, T.G, LDL, and VLDL levels coupled with reduced HDL, is a common feature of obesity and is associated with a raised risk of cardiovascular diseases (CVD) and atherosclerosis. The model control group (G2), which was induced with obesity via a high-fat diet, exhibited significant dyslipidemia, with increases in T.C (116.48%), T.G (76.66%), and LDL (297.78%), alongside a decrease in HDL (-20.8%) and a slight rise in VLDL (41.90%), mirroring the typical lipid imbalances seen in obese animal models. Results align with observations from previous studies that reported similar lipid alterations in high-fat diet-induced obesity models [59,62,63,64,65,67].

These lipid disturbances suggest impaired lipid metabolism, which heightens the risk of cardiovascular complications. Treatment with WRP showed a dose-dependent improvement in lipid profiles. In the 5% WRP group (G3), a moderate reduction in T.C (-26.73%), T.G (-13.85%), and LDL (-37.59%) was observed, alongside a modest increase in HDL (+9.15%) and VLDL (+14.16%). These improvements suggest that WRP may help mitigate hyperlipidemia by exerting antioxidant and anti-inflammatory effects that counteract the oxidative stress and inflammation underlying lipid imbalances in obesity [71,72]. The 10% WRP group (G4) showed even more significant improvements: T.C decreased by 57.41%, T.G by 41.94%, LDL by 79.21%, HDL increased by 21.13%, and VLDL decreased by 42.16%, emphasizing WRP's potential as an effective dietary intervention for obesity-related dyslipidemia and cardiovascular disease prevention. Similarly, DSP also demonstrated beneficial effects on lipid metabolism, though its impact was somewhat less pronounced than WRP's. In the 5% DSP group (G5), T.C was reduced by 50.92%, T.G by 41.91%, and LDL by 70.54%, with a slight increase in HDL (+24.27%) and a notable decrease in VLDL (-42.13%). Results align with observations from studies highlighting the lipid-lowering effects of date seed extracts, credited to their polyphenolic bioactive compounds and other constituents that modulate lipid metabolism and alleviate oxidative stress [25,59,73]. The 10% DSP group (G6) exhibited a reduction in T.C (-37.56%), T.G (-27.09%), and LDL (-52.75%), with a rise in HDL (+17.40%) and a reduction in VLDL (-27.36%), showcasing DSP's potential in improving lipid profiles and mitigating obesity-related cardiovascular risks, albeit with slightly less pronounced effects than WRP. These findings collectively suggest that both WRP and DSP can significantly improve lipid metabolism, offering potential therapeutic benefits for managing obesity-induced dyslipidemia along with lowering the risk of cardiovascular illnesses.

The lipid-lowering effects observed in this study align with results from several other studies on the impact of

natural products on obesity-induced dyslipidemia in rats. The high-fat diet-induced model used in the control group (G2) produced expected lipid disturbances, as seen in various other studies [59,62] [63,64] [65,67]. These authors also reported significant increases in T.C, T.G, and LDL, as well as decreases in HDL levels, when rats were subjected to high-fat diets. The beneficial effects of watermelon peel and date seed powders on lipid profiles in this study are consistent with their documented antioxidant properties, which help reduce oxidative stress and modulate lipid metabolism [58,73].

Numerous studies have examined the potential of watermelon peel and date seed extracts in improving lipid profiles in metabolic disorders. For example, Mahran et al., [58] demonstrated that watermelon peel extract has strong antioxidant activities that can alleviate obesity-related liver damage, which may extend to improving overall lipid metabolism. Likewise, Elmaadawy et al., [73] pointed out that date seed extract exhibited protective effects on liver function and lipid profiles in obese rats. The findings in the current study corroborate these results, particularly in the significant reduction of LDL and triglycerides and the increase in HDL levels with WRP and DSP treatment. Additionally, studies on date seeds have shown their bioactive compounds, such as flavonoids and tannins, help in reducing lipid accumulation and improve HDL levels, which was also evident in the current study with DSP [59,78]. Likewise, the significant dose-dependent improvements in lipid profiles observed with watermelon rind powder (especially in the 10% dose group) are in line with similar studies demonstrating the efficacy of polyphenol-rich plant extracts in reducing hyperlipidemia [58,71].

The reductions in T.C, T.G, and LDL levels, along with the increases in HDL levels in the WRP and DSP-treated groups, can be explained by the presence of bioactive compounds in both watermelon peel and date seed powders. These compounds, including polyphenols, flavonoids, and dietary fibers, are known for their antioxidant, anti-inflammatory, and lipid-modulating properties [82,99,101]. They can enhance the activity of enzymes involved in lipid metabolism, such as lipoprotein lipase, and reduce the activity of enzymes that promote cholesterol synthesis, such as HMG-CoA reductase. Furthermore, these bioactive compounds may improve insulin sensitivity, which is crucial for lipid homeostasis in obesity [59,78]. The significant improvements observed with higher doses of WRP and DSP indicate a dose-dependent response, with greater doses potentially leading to enhanced bioavailability and effects. The more pronounced improvements in the WRP groups, especially in HDL levels, may be due to its higher carotenoid content, particularly lycopene, which has been shown to improve HDL levels and reduce LDL oxidation [19,82,98].

3.8. The Effect of a 10-week Treatment with Watermelon rind (WRP) and Date Seed (DSP) Powders on Kidney Functions of Obese Rats

Table 7. Impact of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on serum lipid profile of obese rats

Groups	T.C (mg/dL)	T.G (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
G1: Normal control	115.17 ^d ±11.68 (0.00)	104.30 ^d ±5.58 (0.00)	51.11 ^a ±0.80 (0.00)	43.26 ^d ±10.03 (0.00)	26.06 ^{bc} ±7.47 (0.00)
G2: Model control	249.33 ^a ±10.30 (116.48)	184.26 ^a ±5.33 (76.66)	40.45 ^e ±1.65 (-20.8)	172.08 ^a ±11.78 (297.78)	36.98 ^a ±1.19 (41.90)
G3 (WRP, 5%)	182.66 ^b ±12.13 (-26.73)	158.73 ^b ±10.47 (-13.85)	44.15 ^d ±0.99 (9.15)	106.77 ^b ±11.67 (-37.59)	31.74 ^b ±2.095 (14.16)
G4 (WRP, 10%)	106.166 ^d ±7.95 (-57.41)	106.97 ^d ±16.12 (-41.94)	49.00 ^b ±0.790 (21.13)	35.76 ^d ±8.91 (-79.21)	21.39 ^c ±3.22 (-42.16)
G5 (DSP, 5%)	122.36 ^d ±9.37 (-50.92)	107.033 ^d ±6.25 (-41.91)	50.27 ^{ab} ±0.90 (24.27)	50.68 ^d ±8.56 (-70.54)	21.40 ^b ±1.25 (-42.13)
G6 (DSP, 10%)	155.66 ^c ±12.19 (-37.56)	134.33 ^c ±11.81 (-27.09)	47.49 ^c ±0.52 (17.40)	81.30 ^a ±10.30 (-52.75)	26.86 ^{bc} ±2.37 (-27.36)

The results are expressed as means ± SD (n=6). Statistical significance is indicated by different superscript letters within the same column ($P \leq 0.05$). Values in parentheses represent the percentage of change (%), with comparisons made between the obese (Model) group and the normal group, as well as between the groups treated with plant parts (WRP and DSP) and the obese group. G1 (Normal control) represents healthy rats without treatment; G2 (Model control) includes obese rats induced by a high-fat diet (HFD) with no treatment; WRP and DSP refer to watermelon rind powder and date seed powder, respectively. G3, G4, G5, and G6 are the obese groups treated with WRP and DSP at 5 and 10 g/100g diet concentrations for 8 weeks. "bw" stands for body weight.

Table 8. The effect of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on kidney functions of obese rats

Groups	Uric acid (mg/dL)		Urea (mg/dL)		Creatinine (mg/dL)	
	Means ±SD	% of change	Means ±SD	% of change	Means ±SD	% of change
G1: Normal control	2.82 ^e ±0.164	0.00	25.71 ^e ±3.987	0.00	0.58 ^c ±0.082	0.00
G2: Model control	8.83 ^a ±0.512	213.12	76.88 ^a ±2.942	198.71	1.14 ^a ±0.052	96.55
G3 (WRP, 5%)	7.21 ^b ±0.255	-18.34	69.99 ^b ±5.847	-8.86	0.92 ^b ±0.052	-19.29
G4 (WRP, 10%)	4.73 ^d ±0.187	-46.43	27.61 ^c ±3.056	-64.04	0.65 ^c ±0.054	-42.98
G5 (DSP, 5%)	5.07 ^d ±0.206	-42.58	39.55 ^d ±3.293	-48.50	0.57 ^c ±0.124	-50
G6 (DSP, 10%)	6.16 ^c ±0.225	-30.23	53.08 ^c ±2.597	-30.88	0.86 ^b ±0.021	-24.56

The results are expressed as means ± SD (n=6). Statistical significance is indicated by different superscript letters within the same column ($P \leq 0.05$). Values in parentheses represent the percentage of change (%), with comparisons made between the obese (Model) group and the normal group, as well as between the groups treated with plant parts (WRP and DSP) and the obese group. G1 (Normal control) represents healthy rats without treatment; G2 (Model control) includes obese rats induced by a high-fat diet (HFD) with no treatment; WRP and DSP refer to watermelon rind powder and date seed powder, respectively. G3, G4, G5, and G6 are the obese groups treated with WRP and DSP at 5 and 10 g/100g diet concentrations for 8 weeks. "bw" stands for body weight.

Table 8 presents the impacts of a 10-week treatment with watermelon rind powder (WRP) and date seed powder (DSP) on kidney function in obese rats, focusing on key renal biomarkers: uric acid, urea, and creatinine. These markers are commonly altered in obesity and metabolic disorders, reflecting impaired renal filtration and excretion. Kidney dysfunction, especially in the context of obesity, is often characterized by elevated levels of these biomarkers, signaling renal stress and injury. The data from the study suggest that both WRP and DSP have beneficial effects on kidney function, as evidenced by their ability to modify the levels of these biomarkers. The model control group (G2), induced with obesity through a high-fat diet, exhibited significant kidney dysfunction, with uric acid, urea, and creatinine levels increasing by 213.12%, 198.71%, and 96.55%, respectively. These findings are consistent with previous studies reporting renal damage in high-fat diet-induced obesity models, where increased uric acid and urea levels indicate kidney stress, and elevated creatinine levels reflect impaired glomerular filtration [59] [117,118]. This pattern of kidney dysfunction is a hallmark of obesity-related metabolic disturbances, which often involve compromised kidney function. In contrast, treatment with WRP showed a dose-dependent improvement in kidney function. The 5% WRP group (G3) demonstrated

moderate reductions in uric acid (18.34%), urea (8.86%), and creatinine (19.29%), suggesting a beneficial effect of WRP in alleviating renal stress, likely due to its antioxidant properties that reduce oxidative damage and inflammation in the kidneys [19,71] [82,119]. The 10% WRP group (G4) showed more pronounced improvements, with reductions of 46.43%, 64.04%, and 42.98% in uric acid, urea, and creatinine, respectively, indicating that higher doses of WRP may have a stronger protective effect on kidney function. These effects are likely due to the higher concentrations of bioactive compounds, such as polyphenols and flavonoids, known to support renal health and function [71,76] [117,118] [120,121]. Similarly, DSP also demonstrated a positive impact on kidney function, although its effects were somewhat less pronounced compared to WRP. In the 5% DSP group (G5), reductions of 42.58%, 48.50%, and 50% in uric acid, urea, and creatinine were observed, suggesting that DSP offers renal protection, likely due to its rich content of polyphenols and bioactive compounds with antioxidant and anti-inflammatory properties [59,80,82]. The 10% DSP group (G6) also showed improvements, with reductions in uric acid (30.23%), urea (30.88%) and creatinine (24.56%), indicating that higher doses of DSP provide therapeutic benefits, albeit to a slightly lesser extent than WRP. These findings suggest that both WRP and DSP possess potential

as protective agents against kidney dysfunction in obesity, with WRP appearing to be more effective at higher doses.

The data presented in Table 7 aligns with several studies on the renal protective effects of plant-derived compounds. Both WRP and DSP demonstrated significant reductions in renal biomarkers, which is consistent with the growing body of research on the therapeutic potential of natural products in treating obesity-induced kidney dysfunction. For example, studies have shown that polyphenolic compounds found in watermelon and date seeds possess antioxidant and anti-inflammatory properties, which can mitigate the oxidative damage and inflammation associated with obesity and metabolic disorders [59,98,101,121]. In similar studies, plant extracts such as those from pomegranate, hibiscus, gum Arabic, Reishi mushroom and Arak (*Salvadora persica*) have been shown to improve kidney function in obese rats by reducing levels of uric acid, urea, and creatinine [71,87] [118,121] [122,124]. The dose-dependent effect observed with both WRP and DSP further supports the idea that higher concentrations of bioactive compounds provide more significant protective effects, a trend that has been observed in numerous studies exploring the dose-response relationship in natural product-based interventions [123]. Moreover, this study is congruent with findings of Elmaadawy et al., [104], who reported similar improvements in kidney biomarkers after treatment with plant extracts. These studies suggest that natural remedies like WRP and DSP, rich in antioxidants, may offer a viable option for mitigating obesity-related kidney dysfunction, thus reducing the risk of CKD and other related complications.

3.9. Influence of a 10-week Treatment with Watermelon rind (WRP) and Date Seed (DSP) Powders on Glutathione and Antioxidant Enzymes in Liver Tissue of Obese Rat

Table 9 evaluates the influence of a 10-week treatment with watermelon rind powder (WRP) and date seed powder (DSP) on oxidative stress markers, specifically glutathione (GSH) levels and antioxidant enzymes (GSH-Px, CAT, and SOD) in obese rats. These markers are essential indicators of the body's ability to counteract oxidative damage, which is often exacerbated in obesity and metabolic disorders. Oxidative stress, caused by an imbalance between reactive oxygen species (ROS) and antioxidants, has been implicated in the development of numerous obesity-related complications, including cardiovascular diseases, diabetes, and kidney dysfunction. In the model control group (G2), which was induced with obesity through a high-fat diet, significant reductions in antioxidant markers were observed, with a decrease in GSH (-89.59%), GSH-Px (-97.43%), CAT (-85.30%), and SOD (-97.68%). These findings suggest a substantial depletion of the body's antioxidant defenses, a hallmark of oxidative stress in obesity. Elevated oxidative stress has

been linked to lipid peroxidation, mitochondrial dysfunction, and inflammation, all of which lead to the etiology of obesity-related diseases [62,63,64] [65,85,86]. The significant reduction in these antioxidant markers indicates an overwhelmed defense system, further exacerbating the metabolic dysregulation associated with obesity [123]. Treatment with WRP demonstrated a dose-dependent improvement in oxidative stress markers. In the 5% WRP group (G3), GSH increased by 145.36%, GSH-Px by 140%, CAT by 94.81%, and SOD by 90.90%. Although the improvements were notable, they were moderate compared to the higher dose groups. These results suggest that WRP may offer protection against oxidative stress, likely due to its antioxidant and anti-inflammatory properties. Prior studies registered that watermelon peel is rich in polyphenolic compounds, including flavonoids, which are potent antioxidants capable of reducing oxidative damage in various tissues [57,71]. The 10% WRP group (G4) showed more dramatic improvements in all markers: GSH increased by 552.66%, GSH-Px by 871.42%, CAT by 318.30%, and SOD by 915.15%. These significant increases suggest that higher doses of WRP are more effective in boosting antioxidant defense systems, which could mitigate the harmful effects of oxidative stress in obesity [58]. DSP also had a positive impact on oxidative stress markers, though its effects were somewhat less pronounced than those of WRP. In the 5% DSP group (G5), GSH increased by 706.20%, GSH-Px by 2517.14%, CAT by 426.31%, and SOD by 2481.81%. These results demonstrate that DSP is a potent antioxidant, and its bioactive compounds, including polyphenols, flavonoids, and tannins, may play a crucial role in improving oxidative stress markers in obese rats [59,75,78,95,101]. The 10% DSP group (G6) showed reductions in the increases of these markers compared to the 5% DSP group: GSH increased by 315.34%, GSH-Px by 257.14%, CAT by 190.75%, and SOD by 212.12%. Although these improvements were significant, they were not as pronounced as those in the WRP groups. This suggests that while DSP has beneficial antioxidant effects, it may require higher concentrations to achieve a similar level of efficacy as WRP in combating oxidative stress associated with obesity [59,101].

Results from this study align with similar findings in the literature, where natural antioxidants, such as those from watermelon peel and date seeds, have been shown to improve oxidative stress markers in obese and diabetic animal models. The protective impacts of WRP and DSP may be attributed to their polyphenolic content, which has been widely recognized for its ability to scavenge free radicals and reduce oxidative damage [57,59,75] [82,99,101]. Furthermore, the observed dose-dependent effects suggest that higher doses of these natural products may be more effective in boosting antioxidant defenses and mitigating oxidative stress. This study provides promising evidence for the potential of WRP and DSP as functional foods for managing obesity-related oxidative stress and metabolic dysfunction.

Table 9. Influence of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on glutathione and antioxidant enzymes in liver tissue of obese rat

Groups	GSH (mmole /100 g wet tissue)	GSH-Px (U/g wet tissue)	CAT (U/g wet tissue)	SOD (U/g wet tissue)
G1: Normal control	219.9 ^a ±12.42 (0.00)	13.64 ^a ±1.30 (0.00)	224.5 ^a ± 9.09 (0.00)	14.25 ^a ±1.46 (0.00)
G2: Model control	22.88 ^f ±3.17 (-89.59)	0.35 ^d ± 0.04 (-97.43)	32.99 ^f ±5.06 (-85.30)	0.33 ^d ±0.05 (-97.68)
G3 (WRP, 5%)	56.14 ^e ±4.56 (145.36)	0.84 ^d ± 0.05 (140)	64.27 ^e ±10.66 (94.81)	0.63 ^d ±0.06 (90.90)
G4 (WRP, 10%)	149.33 ^c ±8.86 (552.66)	3.40 ^c ±0.64 (871.42)	138 ^c ±7.915 (318.30)	3.35 ^c ±0.62 (915.15)
G5 (DSP, 5%)	184.46 ^b ±4.17 (706.20)	9.16 ^b ±0.94 (2517.14)	173.63 ^b ±6.21 (426.31)	8.52 ^b ±0.84 (2481.81)
G6 (DSP, 10%)	95.03 ^d ±4.75 (315.34)	1.25 ^d ±0.08 (257.14)	95.92 ^d ±3.20 (190.75)	1.03 ^d ±0.06 (212.12)

The results are expressed as means ± SD (n=6). Statistical significance is indicated by different superscript letters within the same column ($P \leq 0.05$). Values in parentheses represent the percentage of change (%), with comparisons made between the obese (Model) group and the normal group, as well as between the groups treated with plant parts (WRP and DSP) and the obese group. G1 (Normal control) represents healthy rats without treatment; G2 (Model control) includes obese rats induced by a high-fat diet (HFD) with no treatment; WRP and DSP refer to watermelon rind powder and date seed powder, respectively. G3, G4, G5, and G6 are the obese groups treated with WRP and DSP at 5 and 10 g/100g diet concentrations for 8 weeks. "bw" stands for body weight.

3.10. Histological studies

3.10.1. Influence of a 10-week Treatment with Watermelon Rind (WRP) and Date Seed (DSP) Powders on Live Histology Tissues of Obese Rat

The Influence of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on liver histology tissues of obese rat was registered in [Figure 2](#). Light microscopic examination of liver sections of rats in group 1 revealed the normal histological architecture of hepatic lobules (Photo 1). In contrast, liver of rats from group 2 showed inflammatory cells infiltration in the portal triad (Photo 5) and slight activation of Kupffer cells (Photo 3). At this point, liver of rats in group 3 showed slight vacuolar degeneration of some hepatocytes (Photo 4). From another direction, some examined hepatic tissue of rats in group 4 exhibited no histopathological alterations (Photo 5). Furthermore, liver of rats in group 5 exhibited steatosis of some hepatocytes (Photo 6). From another direction, some examined hepatic tissue of rats in group 6 showed slight vacuolar degeneration of sporadic hepatocytes (Photo 7). The histopathological findings align with previous studies indicating that HFD-induced obesity leads to hepatic inflammation and lipid accumulation [112,124,126]. The absence of significant histopathological alterations in Group 4 (10% WRP) suggests a hepatoprotective effect, potentially attributed to the antioxidant and anti-inflammatory properties of watermelon rind compounds [18,19]. Similarly, the mild steatosis observed in Group 5 (5% DSP) is consistent with reports highlighting the lipid-lowering effects of date seed extracts [127,128,129]. Yet, the more pronounced vacuolar degeneration in Group 6 (10% DSP) suggests that higher doses may not confer additional hepatoprotective benefits. These findings support the potential of natural plant-based supplements in mitigating obesity-related hepatic complications.

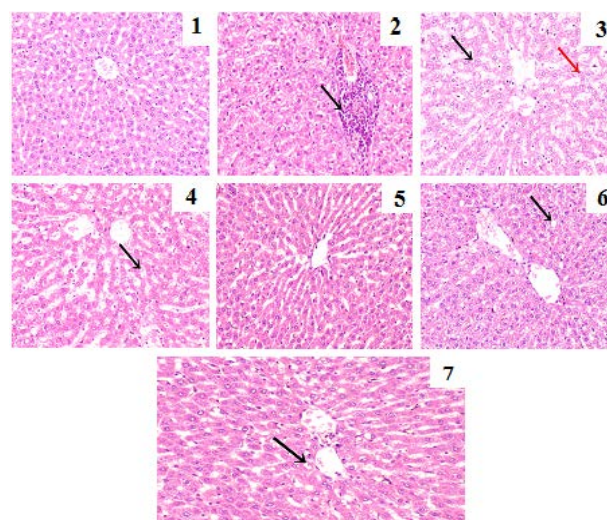


Figure 2. Influence of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on live histology tissues of obese rat

Photo 1. Photomicrograph of liver of rat from group 1 showing the normal histological architecture of hepatic lobule. **Photo 2.** Photomicrograph of liver of rat from group 2 showing inflammatory cells infiltration in the portal triad (arrow). **Photo 3.** Photomicrograph of liver of rat from group 3 showing hepatocellular steatosis of some hepatocytes (black arrow) and slight activation of Kupffer cells (red arrow). **Photo 4.** Photomicrograph of liver of rat from group 5 showing slight vacuolar degeneration of some hepatocytes (arrow). **Photo 5.** Photomicrograph of liver of rat from group 6 showing no histopathological alterations. **Photo 6.** Photomicrograph of liver of rat from group 4 showing steatosis of some hepatocytes (arrow). **Photo 7.** Photomicrograph of liver of rat from group 6 showing slight vacuolar degeneration of sporadic hepatocytes (arrow) (H & E X 400).

3.10.2. Influence of a 10-week Treatment with Watermelon Rind (WRP) and Date Seed (DSP) Powders on Heart Histology Tissues of Obese Rat

The influence of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on heart histology tissues of obese rat was registered in [Figure 3](#). Microscopically, heart of rat in group 1 revealed the normal histological structure of cardiac myocytes (Photo 1). By comparison, heart of rats in group 2 registered vacuolation of the sarcoplasm of cardiac myocytes (Photo 2) and intermyocardial edema dispersed the cardiac myocytes (Photo 3). Furthermore, some sections in group 3 exhibited slight intermyocardial edema (Photo 4). Also, sections in group 4 exhibited no histopathological lesions (Photo 5). At this point, heart tissue of rats in group 5 described no changes except congestion of myocardial blood vessels (Photo 6). Moreover, apparent some heart sections of rats from group 6 showed slight congestion of myocardial blood vessels (Photo 7). The histopathological findings align with previous studies indicating that HFD-induced obesity leads to myocardial injury characterized by vacuolation of cardiac myocytes and intermyocardial edema [\[70,130\]](#). The absence of significant histopathological alterations in Group 4 (10% WRP) suggests a protective effect, potentially attributed to the antioxidant and anti-inflammatory properties of watermelon rind compounds. Similarly, the mild circulatory disturbances observed in Groups 5 and 6 (DSP supplementation) are consistent with reports highlighting the vascular benefits of date seed extracts [\[107,129\]](#). Support these findings on the possibility of natural plant-based supplements in mitigating obesity-related cardiac complications.

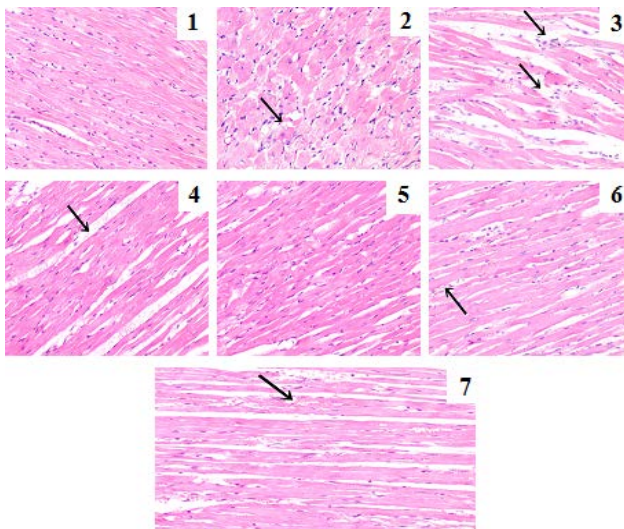


Figure 3. Influence of a 10-week treatment with watermelon rind (WRP) and date seed (DSP) powders on heart histology tissues of obese rat

Photo 1. Photomicrograph of heart of rat from group 1 showing the normal histological structure of cardiac myocytes. **Photo 2.** Photomicrograph of heart of rat from group 2 showing vacuolation of the sarcoplasm of cardiac myocytes (arrow). **Photo 3.** Photomicrograph of heart of rat from group 2 showing intermyocardial edema dispersed the cardiac myocytes (arrow). **Photo 4.** Photomicrograph of heart of rat from group 4 showing

slight intermyocardial edema (arrow). **Photo 5.** Photomicrograph of heart of rat from group 4 showing no histopathological lesions. **Photo 6.** Photomicrograph of heart of rat from group 3 showing congestion of myocardial blood vessel (black arrow). **Photo 7.** Photomicrograph of heart of rat from group 5 showing slight congestion of myocardial blood vessel (black arrow) (H & E, X 400).

4. Conclusion

The current study demonstrates that watermelon rind powder (WRP) and date seed powder (DSP) effectively reduce body weight gain, feed intake, and improve feed efficiency in obese rats. These effects may be attributed to the bioactive components in both powders, which offer benefits such as appetite suppression, improved fat metabolism, and antioxidant properties. While WRP appears to be more effective, especially at higher doses, DSP also shows beneficial effects, particularly in improving kidney and heart weight. Both WRP and DSP have potential as natural interventions to reduce obesity-induced organ hypertrophy and liver dysfunction. The data suggest significant hepatoprotective effects, with WRP having a stronger impact on reducing liver enzyme levels compared to DSP. Both treatments exhibited significant reductions in ALT, AST, and ALP, indicating their therapeutic role in managing obesity-related liver dysfunction. Additionally, both WRP and DSP demonstrated significant reductions in bilirubin levels, further supporting their hepatoprotective effects. These findings are highlighting the antioxidant and anti-inflammatory effects of watermelon peel and date seed extracts, contributing to improved liver health. The 10-week treatment with these powders improved blood glucose, insulin, and leptin levels in obese rats, with DSP showing more pronounced effects at lower doses. This suggests that both natural treatments have potential to improve metabolic health, particularly in the context of obesity and metabolic disorders. Furthermore, both WRP and DSP demonstrated substantial benefits in improving lipid profiles by reducing total cholesterol, triglycerides, and LDL, while increasing HDL levels, suggesting their effectiveness in counteracting dyslipidemia and reducing cardiovascular risks. The improvements in kidney function markers, such as reduced levels of uric acid, urea, and creatinine, indicate that these natural products could serve as effective dietary supplements for combating obesity-induced renal dysfunction. While WRP appears to be more effective than DSP, especially at higher doses, the findings are consistent with the growing body of literature supporting the use of plant-derived compounds in treating obesity-related metabolic disorders. The dose-dependent effects observed in this study suggest that higher doses of these natural products may be more effective in boosting antioxidant defenses and mitigating oxidative stress, supporting the use of WRP and DSP as potential functional foods or nutraceuticals for improving antioxidant status and reducing oxidative damage in obesity. More research is required to understand the molecular mechanisms behind these effects and explore the clinical applications of these powders in human subjects.

Conflict of Interests

Authors declared no competing interest whatsoever.

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Authors' Contribution

Yousif Elhassaneen played a central role in formulating the research protocol, supervising the laboratory procedures, gathering conceptual data, verifying the findings and statistical outputs, and preparing the initial manuscript draft along with conducting a comprehensive critical revision. Asmaa Elgarf was responsible for carrying out the experimental work, organizing and analyzing the data, interpreting the results, and contributed to the conceptual framework and manuscript drafting. Amal Nasef Zaki participated in designing the study framework, sourcing background information, contributing to the study's design and rationale, validating the findings, and drafting the manuscript.

Abbreviations

AA, antioxidant activity, Abs, absorbance, Alb, albumin, ALP, alkaline phosphatase activity, ALT, alanine aminotransferase activity, AST, aspartate aminotransferase activity, BWG, body weight gain, CAT, catalase, D.B, direct bilirubin, DSP, date seed powder, FI, feed intake, G6PD, glucose-6-phosphatase, FER, feed efficiency ratio, GGT, Gamma-Glutamyl Trans peptidase, GSH, reduced glutathione, GSH-Px, glutathione peroxidase, GSSG, oxidized glutathione, HDL-c, High density lipoprotein-cholesterol, HFD, high-fat diet, ID. B, indirect bilirubin, LDL-c, low density lipoprotein-cholesterol, MDA, malondialdehyde, MLP, mulberry leaves powder, ROS, reactive oxygen species, WRP, watermelon rind powder, SD, standard deviation, SOD, Superoxide dismutase, T.B, total bilirubin, TGs, triglycerides, T.P, total protein.

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