Potential Effects of Ethanolic Extracts of *Capsicum annuum* L. and *Cucumis melo var. flexuosus* Seeds on Obesity and its Complications Caused by High-Fat Diet in Rats : A Comparative Study

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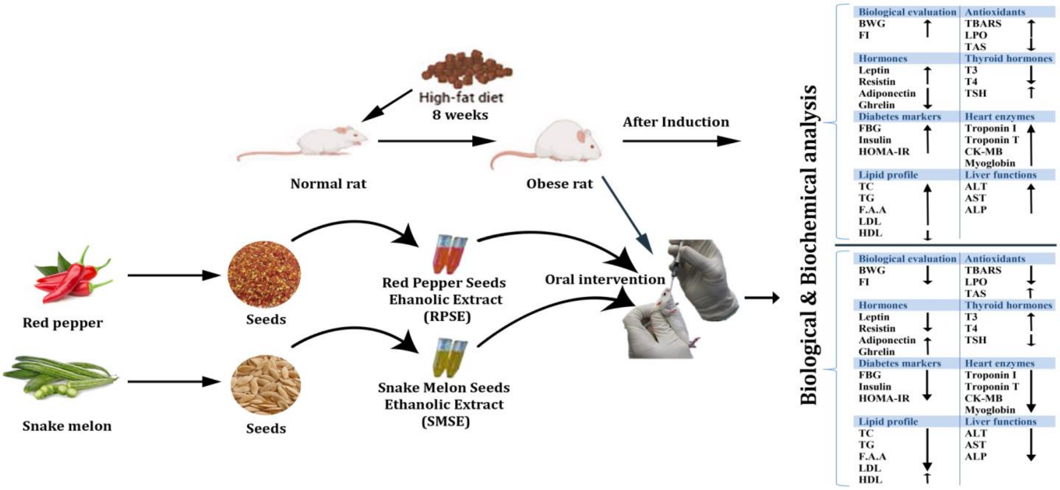
Abstract: Obesity is a chronic condition affecting more than one-third of the global population. It causes a burden on human health in both developed and developing countries. Currently, there is an increasing need for effective natural obesity therapies. Plant seeds have received a lot of attention recently due to their efficiency and biocompatibility.Therefore, the purpose of this study was to know the potential effects of red pepper seed extract (RPSE) and snake melon seed extract (SMSE) on obesity and its complications in rats. By analyzing the biologically active components of RPSE and SMSE, it was found that RPSE contains higher concentrations of phenolic active compounds than SMSE.On the other side, the biological experiment indicated that feeding normal rats an 4-week high-fat diet (model control) resulted in considerably ($p \leq 0.05$) higher body weight gain, feed intake, and feed efficiency ratio when compared to the normal group. However, after four weeks of feeding obese rats with concentrations of 250 and 500 mg/kg body weight of both RPSE and SMSE, the serum lipid profile parameters significantly ($p \leq 0.05$) improved .Also, the liver functions, cardiac enzymes (troponin, CK-MB, myoglobin), thyroid hormones (T3, T4, TSH), levels of TBARS, LPO, total antioxidants (TAS), diabetic phenotypes(FBG, HOMA-IR, insulin levels) , hormones satiety and hunger (leptin, ghrelin), and plasma levels of the hormone adiponectin and resistin were improved when compared to the model group. But, the effect of RPSE on previous markers was better than SMSE. Therefore, this study recommends the possibility of adding red pepper seeds to nutritional supplements to prevent obesity and its complications **.**

Keywords : adipokines , cardiac biomarkers, HOMA-IR , lipid peroxidation, snake melon, red chili pepper

Graphical abstract



1.Introduction

The rising incidence of obesity worldwide poses a serious public health concern, mainly due to lifestyle factors such as high-fat meals and sedentary behaviors that impact both adults and children **(Elebeedy *et al.*, 2022 & Ugbaja *et al.*, 2020).** More than 167 million people are expected to experience obesity-related health difficulties by 2025, according to the World Health Organization (WHO), which forecasts a startling rise in these conditions **(Shagdarova *et al.*, 2023).** Numerous health issues are associated with this epidemic, such as nonalcoholic fatty liver disease (NAFLD), metabolic syndrome, diabetes, hypertension, and heart disease **(Elebeedy *et al.*, 2022, Tang *et al.*, 2020 and Shagdarova *et al.*, 2023).** Because synthetic anti-obesity medications have side effects, researchers are looking to natural substances that have comparable effects. Using medicinal or functional food plants or their chemicals, which naturally reduce weight and fat production, is one way to prevent and treat these dysfunctions **(Sung *et al.*, 2018 and Azlan *et al.*, 2022)**.

One such promising plant might be the snake melon, along with red pepper. One of the most widely eaten spices worldwide is chili pepper (*Capsicum annuum*), which is used in a variety of dishes for flavor, scent, and to prevent food from spoiling. It is also employed in the pharmaceutical and food sectors because of its high vitamin C content **(Zhang *et al.*, 2024)**. Due to its well-regarded medical qualities, which include anti-obesity as well as anti-inflammatory, anti-analgesic, anti-diabetic, antilipidemic, and anti-cancer benefits **(Lu *et al.*, 2020)**.

Although much research has been done on the pulp of red peppers, their seeds were considered only a valuable by-product. In a recent study, red pepper seeds decreased fat accumulation in vitro by suppressing the expression of important adipogenic transcription factors in 3T3-L1 adipocytes, including peroxisome proliferator-activated receptor γ (PPARγ) and CCAAT/enhancer-binding protein α (C/EBPα) **(Irandoost *et al.*, 2021)**. Because red pepper seeds are antioxidant and improve radical scavenging, they also have anti-mutagenic qualities **(Ertekin and Keçeci 2022)**. Red pepper seeds reduced oxidative damage in rats fed high-fat diets by activating antioxidative defense systems such as superoxide dismutase and catalase **(Irandoost *et al.*, 2021).**

In many regions of the world, snake melon (*Cucumis melo,* var. flexuosus (L.), Cucurbitaceae family) is an old crop. It is one of the natural antioxidants used in medicine and can be eaten raw in salads**(Ilahy *et al.*, 2022)**. Its antioxidant properties are caused by a variety of bioactive phytochemicals, including phenolic compounds, tannins, alkaloids, and flavonoids **(Sayyar *et al.*, 2023**). Snake melon is gaining popularity because of their high nutritional content. According to **Rolnik and Olas (2020).** Snake melon is mostly composed of water (96%) with 1.2% protein, 4.5% carbohydrates, 0.7% fat, and 2% fiber. According to **Sayyar *et al.*,(2023).** Snake melon is a noteworthy provider of several minerals, including potassium (264%), phosphorus (37%), calcium (33%), magnesium (27%), and sodium (25%), as well as vitamins, primarily vitamin C (21.3%). Additionally, polyphenols, lutein (165%), beta-carotene (14%), and vitamin A (12%)**(Sereno *et al.*, 2022)**. Based on the foregoing and as a continuation of earlier research, the objective of this work was to assess the possible effects on obese rats of ethanolic extracts from red pepper and snake melon seeds by assessing body weight gain, lipid levels, oxidative stress, diabetic phenotypes, and the biochemical functions of the liver and heart. This was done in an effort to clarify any beneficial and detrimental effects.

2. Materials and Methods

2.1. Materials

2.1.1. Collection, identification, and authentication

The red chili pepper and snake melon were acquired at Galhoum supermarket in Shebin El-koum, El-Menoufia, Egypt. The fruits were collected in plastic thread bags and validated by plant taxonomy professors at Menoufia University's Faculty of Agriculture in Shebin El Kom, Egypt.

2.1.2. Chemicals and diets

Alkan Medical Company, based in St. El Doky, Giza, Egypt, supplied biochemical assay kits. The El-Gomhoreya Company in Cairo, Egypt, provided all further chemicals, and reagents used in this experiment.

High-fat-Diet (HFD) composition: HFD comprised of normal chew (54%), sucrose (15%), lard (15%), egg yolk powder (5%), milk powder (4%), peanut (3%), salt (2%), sesame oil (1%), dicalcium phosphate (0.6%), and mountain flour (0.4%) as described by **Ghoneim *et al.*, (2024).**

Basal diet (BD): The basal diet was prepared from fine ingredients in accordance with **Reeves *et al*., (1993)** as follows: protein (casein) 12%, sunflower oil 10%, cellulose 5%, DL-methionine 0.3%, choline chloride 0.2%, vitamin mixture 1% , salt mixture 4% and corn starch up to 100 g. The componentof the mineral and vitamin mixture that was employed was prepared in accordance with **Reeves *et al*., (1993)**

2.2. Methods

2.2.1. Preparation of red pepper seeeds ethanol extracts (RPSE)

A grinder was utilized to smash the dried red pepper seeds, which were then incorporated in the cold-storage samples. After combining the crushed pepper seeds with six batches of 100% ethanol, the extraction process was run for twenty-four hours at 4 °C. After three iterations of this procedure, the top liquid was gathered and filtered using filter paper. A rotary evaporator was used to evaporate the solvent of the combined extracts at low pressure, and a freeze dryer was used to dry them **(Song *et al.*, 2010).**

2.2.2. Preparation of snake melon seeds ethanol extracts (SMSE)

Snake melon seed extract (SMSE) was prepared according to the previous description of **Sayyar *et al.*, (2023)**.To put it briefly, the seeds of the snake melon were separated, dried under shade, and then coarsely ground using an electric blender (Moulinex, France). The powdered form (powder to solvent ratio: 1:10 w/v) was soaked in ethanol for 24 hours at 37–40°C while being constantly stirred. In a rotary evaporator operating at 45 to 50°C and low pressure, the solvent was evaporated. Snake melon residue, which was semisolid and dark brown in final extract yield (19.24%), was kept in an airtight container at 4°C until it was needed.

2.2.3. Quantitative determination of phenolic compounds by HPLC

The total phenolic content of the samples (RPSE and SMSE) were evaluated with the Folin-Ciocalteu technique **(Eom *et al.*, 2012).** An Agilent 1260 series was used for the HPLC analysis. For separation, the Zorbax Eclipse Plus C8 column (4.6 mm x 250 mm i.d., 5 μm) was used. The mobile phase was made up of water (A) and 0.05% trifluoroacetic acid in acetonitrile (B), and it ran at a rate of 0.9 ml/min. For the mobile phase, the sequential linear gradient programming looked like this: 82% A for 18–22 minutes, 82% A for 22–24 minutes, 82% A for 0–1 minute, 75% A for 1–11 minutes, 60% A for 11–18 minutes, and 82% A for 0 minute. The multi-wavelength detector was observed at 280 nm. Five microliters was the injection volume for each sample solution. The column temperature stayed constant at 40°C.

2.2.4. Biological Experimental

2.2.4.1. Ethical Approval

The experimental and animal care protocol has been authorized ethically by the Institutional Animal Care and Use Committee (IACUC) of Menoufia University, Sheibin El-Kom, Egypt (Approval No. MUFHE/F/NFS/34/24).

2.2.4.2. Animals

The study utilized 36 adult male albino rats weighing 140±10 g each, which were acquired from the National Research Center's animal housing unit in Giza, Egypt.

2.2.4.3. Experimental Design

A twelve-hour light-dark cycle and a temperature-controlled environment (22 ± 1°C) with a relative humidity of 55 ± 10% were provided for the 36 male Sprague Dawley rats. Each male rat weighs 140±10 g. They had unlimited access to water and a BD. Following a week-long acclimation phase, the rats were split into two primary groups: **first main group**, (n=6 rats); a normal control group, fed on BD over the experimental period (8 weeks), The **second main group**, (n=30 rats); was fed on HFD for 4 weeks to induce obesity as described by **Ghoneim *et al.*, (2024),** and then rats were classified into five equal subgroups as follows: **group 2.** as a positive control group, fed on HFD, **groups 3 and 4.** fed on HFD and given a daily dose of 250 mg/kg bw of RPSE and 250 mg/kg bw of SMSE, respectively for another 4 weeks. **groups 5 and 6.** fed on HFD and given a daily dose of 500 mg/kg bw of RPSE and 500 mg/kg bw of SMSE, respectively for another 4 weeks. The rats in every group had been their daily food consumption documented, and every week their body weight was checked. At the end of the period, all rats were undergoing an overnight fast followed by an intraperitoneal injection of 50 mg/kg thiopental sodium to induce anesthesia for the purpose of taking blood samples and conducting biological and biochemical analyses**.**

2.2.5. Biological Evaluation

According to **Chapman *et al.*, (1959)**, the body weight gain (BWG), feed intake (FI), and feed efficiency ratio (FER) were calculated using the following formulas: FER = Grams gain in body weight (g/day)/Grams feed intake (g/day), and BWG = (Final weight minus Initial weight).

2.2.6. Blood Sampling

Following the 4-week experimental phase, rats were anesthetized with thiopental sodium, and blood samples were taken from the abdominal aorta following a 12-hour fast. According to **Stroev and Makarova's (1989)** instructions, blood samples were drawn into sterile, dry centrifuge tubes, allowed to clot at room temperature, and then centrifuged for 10 minutes at 3000 rpm in order to separate the serum. Before being analyzed, the serum was carefully extracted, moved to sterile, clean tubes, and frozen at -20°C.

2.2.7. Hematological Analysis

2.2.7.1. Hormones determination

Plasma leptin and adiponectin levels were determined using ELISA (catalog numbers 90040 and 80570, respectively, Crystal Chem, Downers Grove, IL) **(Bruder *et al.,* 2005)**. Plasma resistin was tested using ELISA (catalog number RD391016200R, BioVendor, Karasek, Czech Republic). The Rat Acylated Ghrelin Express Elisa kit (catalog number RA394162405R) was used to evaluate ghrelin plasma levels.

2.2.7.2. Fasting blood glucose (FBG)

Every two weeks, a blood glucose test meter was used to measure the FBG levels in the tail vein, using the Rat Glucose Assay kit (Crystal Chem, IL, USA).

2.2.7.3. Insulin and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) determination

Following the manufacturer's instructions and using a rat-specific insulin ELISA kit (EMD Millipore, USA) to quantify the blood insulin concentration, HOMA-IR was computed using the following formula **(Caumo *et al.,* 2006)**. HOMA-IR = fasting serum insulin (µIU/ml) x fasting serum glucose (mg/dl) /405.

2.2.7.4. Serum Lipid Profile

Total cholesterol, triglycerides, low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were determined in serum according to the methods of **Richmond, (1973)**, **Fossati and Prencipe, (1982)**, **Islam *et al.,* (2022)** and **Lopes-Virella *et al.,* (1977)**

2.2.7.5. Oxidative Stress Determination

As stated in commercial kit package inserts **(Kandır, 2015 and Messarah *et al.,* 2011)**, the levels of plasma total antioxidant status (TAS) and thiobarbituric acid reactive substances (TBARS) were evaluated using a colorimetric approach utilizing the Biotek brand ELX800 model ELISA instrument.A colorimetric technique for determining the amount of lipid peroxidation (LPO) in serum samples was presented by **Tateishi *et al.,* (1987).**

2.2.7.6. Thyroid hormones

The quantities of triiodothyronine (T3) and thyroxin (T4) were measured according to **Paczkowska *et al.*, (2020)** .Thyroid-stimulating hormone (TSH) was also measured according to **Henning *et al.*, 2014).**

2.2.7.7. Heart function

Creatine Kinase (CK), myoglobin (MB) and cardiac troponin I and troponin T were detected following the procedures of **Tateishi *et al.*, (1987); Walker *et al.*, (1990) and Omole *et al.*, (2018)**, respectively.

2.2.7.8. Liver Functions

According to **Tietz (1976), Yound (1975), and Vassault *et al.*, (1999)**, serum levels of the enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) were examined.

2.2.8. Statistical Analysis

A automated Costat program with a one-way ANOVA was used to statistically analyze all of the data. The mean ± standard deviation (SD) was used to display the results. Significant changes between treatments were indicated by P-values ≤ 0.05. **(Snedecor & Cochran, 1967)**

3. Results and discussion

3.1. The most phenolic active compounds found in red pepper and snake melon seeds

The most phenolic active ingredients in red pepper and snake melon seeds are listed in Table 1. The table shows that, in contrast to snake melon seeds, which have fewer of these potent components, the most prevalent phenolic compounds identified in red pepper seeds are ellagic acid, chlorogenic acid, coffeic acid, cinnamic acid, and daidzein. Perhaps the increased concentration of these active phenolic compounds in red pepper seeds compared to snake melon seeds is what explains the positive active results that the research reached for red pepper seeds compared to snake melon seeds.

These findings are entirely consistent with **Echave *et al.*, (2020),** who found that pepper seeds are high in volatile chemicals and a strong source of carotenoids, phenolic acids, flavonoids, and vitamins C, E, and A. The two distinct alkaloids in this genus, capsaicinoids and capsinoids, have been linked to several beneficial pharmacological and biological effects, such as anti-inflammatory and antioxidant properties. **Lidikova *et al.*, (2021)** investigated the pepper's total polyphenol content, vitamin C content, and capsaicin content.

Additionally, **Sayyar *et al.*, (2023**) demonstrate that the *Cucurbitaceae* family, which includes snake melon contains a variety of vital phytoconstituents, such as flavonoids, alkaloids and saponins. These compounds possess anti-inflammatory, antioxidant, antibacterial, antifungal, antiviral, antiulcer, antihypertensive, and antiangiogenic qualities.

Table (1) : The most important phenolic active compounds found in red pepper and snake melon seeds (µg/g)

Phenolic compounds	red pepper seeds	snake melon seeds	Phenolic compounds	red pepper seeds	snake melon seeds
	Conc. (µg/g)	Conc. (µg/g)		Conc. (µg/g)	Conc. (µg/g)
Gallic acid	29.39	37.43	**Vanillin**	9.65	14.93
Chlorogenic acid	68.88	40.21	**Ferulic acid**	6.01	0.00
Catechin	0.00	0.00	**Naringenin**	12.81	4.79
Methyl gallate	2.54	1.05	**Rosmarinic acid**	7.33	0.00
Coffeic acid	27.04	7.60	**Daidzein**	19.39	10.06
Syringic acid	16.16	6.90	**Querectin**	6.85	14.07
Rutin	0.00	6.56	**Cinnamic acid**	3.91	0.91
Ellagic acid	137.61	0.00	**Hesperetin**	0.00	0.82

3.2. Effect of red pepper and snake melon seeds ethanolic extract on feed intake (FI), feed efficiency ratio (FER) and body weight gain (BWG) of obese rats

The impact of red pepper and snake melon seeds ethanolic extracts on feed intake (FI), feed efficiency ratio (FER) and body weight gain (BWG) of obese rats is displayed in Table 2 . The results of the table demonstrated that the obese rats group showed significantly ($p \leq 0.05$) higher FI (57.78%) , FER (53.12%) and BWG (141 %) compared to the normal group . On the other hand , values of FI, FER and BWG of obese rats were significantly ($p \leq 0.05$) decreased after receiving red pepper and snake melon seeds ethanolic extracts (250 and 500 mg/kg BW) for 28 days . The percentage of decreases reached -27.61 , -7.14 and -32.64% ,-32.70, -30.61 and -53.36 % , -8.13 , -2.04 and -9.84% and -16.78, -

5.10 and -20.72 % compared to the model group, respectively. The groups treated with pepper seeds recorded the best results compared to the snake melon groups, which showed a less effective effect.The highest concentration of pepper seeds (500 mg / kg BW) showed the best results compared to all treatments used.

These findings are in line with **Wang *et al.*, (2020),** who demonstrated that a higher body weight, BMI, and risk of overweight and obesity were linked to higher fat intake and high-fat diets. Furthermore, a high-fat diet (HFD) is the most common cause of obesity, according to **Syarif *et al.*, (2024).**

Feeding rats on pepper seeds extracts showed positive results , these findings are in line with **Zhang *et al.*, (2024)** who showed that capsaicin, which is present in red pepper seeds, can aid in weight loss and may be helpful in treating rat obesity. Capsaicin can cause weight loss because it triggers the release of catecholamine from catecholaminergic neurons in the brain's rostral ventrolateral medulla **(Akabori et al., 2007) .**

According to **Ludy and Mattes (2011)** and **Zanzer *et al.*, (2018),** persons who consumed capsaicin on a regular or occasional basis had less hunger for food that was high in fat, savory, or sugary. **Tobolka *et al.*, (2021)** investigated various pepper parts to identify the part with the highest capsaicin concentration and they found that the fleshy part of the pepper contained little capsaicin; the pepper seeds contained larger amounts. The membrane within the pepper pod where the seeds are connected has the highest concentration of capsaicin. Furthermore, large-scale multicentric studies confirmed that eating capsaicinoids lowers weight, belly fat stores, appetite, and food intake. Consequently, capsaicinoids can be a useful addition to meals and a dietary supplement in diet plans that aim to increase metabolism and reduce body weight **(Irandoost *et al.*, 2021).** However, clinical trials did not demonstrate that non-pungent capsinoids significantly affect human weight and obesity, in contrast to red pepper and capsaicin **(Elmas and Gezer, 2022 ; Szallasi 2022).**

Also, the groups of rats treated with snake melon seeds showed good results, even if they were less than the results of red pepper seeds. Members of the *Cucurbitaceae* family, such as snake melon are known for their health advantages since they are high in dietary fiber and protein. Furthermore, their seeds include vital elements like minerals, copper, phosphorus, zinc, and more according to **Rolnik and Olas (2020). Jenko Pražnikar *et al.*, (2023)** reported that eating more dietary fiber may be a practical way for obese and overweight people to lose weight and improve their metabolic health. Additionally, **Hebbar *et al.*, (2024)** demonstrated that improving dietary fiber intake can enhance weight, body composition, and insulin resistance .

Table (2): Effect of red pepper and snake melon seeds ethanolic extract on feed intake (FI), feed efficiency ratio (FER) and body weight gain (BWG) of obese rats

Groups	FI (g/ day)		FER		BWG (g/ day)	
	Mean ± SD	change%	Mean ± SD	change%	Mean ± SD	change%
G1	12.46±.81[c]	---	0.064 ± 0.004[b]	-----	0.8±0.1[e]	----
G2	19.66 ± 1.38[a]	57.78	0.098 ± 0.004[a]	53.12	1.93± 0.052[a]	141.25
G3	14.23 ±.960[c]	-27.61	0.091± 0 .007[a]	-7.14	1.3± 0.1[d]	- 32.64
G4	18.06 ±.737[ab]	-8.13	0.096 ± 0.001[a]	-2.04	1.74± 0.055[b]	-9.84
G5	13.23 ±.960[c]	-32.70	0.068 ± 0.012[b]	-30.61	0.9±0.1[e]	-53.36
G6	16.36 ±.850[b]	-16.78	0.093± 0.008[a]	-5.10	1.53±0.152[c]	-20.72
LSD	**1.73**	**-----**	**0.013**	**----**	**0.177**	**-----**

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different (p≤ 0.05). G1, Normal control: healthy rats without intervention; G2, Model control fed on HFD for 4 weeks for obesity, then switched to be fed on BD for another 4 weeks; G3and G5, Obese rats received 250 and 500 mg/kg bw of RPSE, respectively; G4 and G6, Obese rats received 250 and 500 mg/kg bw SMSE, respectively. RPSE, red pepper seeds extract ; SMSE, snake melon seeds extract ; FI, feed intake; FER, feed efficiency ratio; BWG, body weight gain.

3.3. Effect of red pepper and snake melon seeds extracts on leptin, adiponectin , resistin and ghrelin hormones of obese rats.

Table 3 displays the impact of red pepper and snake melon seeds extracts on leptin , adiponectin , resistin and ghrelin hormones of obese rats. Our model group showed a considerable (p≤0.05) increase in leptin (1980.5%) and resistin (93.97%) as compared to normal rats. In contrast, the model group showed a considerably (p ≤0.05) lower adiponectin (-82.82%) and ghrelin (-83.09%) than the normal rats.Obese rats showed significant (p≤ 0.05) decreases in their leptin and resistin values after feeding on red pepper and snake melon seeds extracts (250 and 500 mg/kg BW) for 28 days, as compared to the model group. The decreases were -64.96 and -84.28% , -26.81and - 49.81% , -34.18, -44.49 % and - 9.60 and -24.71% , in that sequence .

On the contrary, the adiponectin and ghrelin values of obese rats were significantly ($p \leq 0.05$) higher than those of the model group after feeding on red pepper and snake melon seeds extracts (250 and 500 mg/kg BW) for 28 days. The increases were 215.64 and 420.94% ,16.34 and 57.82 % , 299.14% , 343.59% and 136.90% in that order. The group treated with pepper seeds at a concentration of (500 mg / kg BW) showed the best results compared to the groups treated with snake melon seeds. These findings are in line with those of **Liu *et al.,* (2020)**, who found that two traits of typical obesity are resistance to body mass reduction and hyperleptinemia. When compared to T2DM patients with normal BMI, obese patients showed a disrupted adipocytokine profile, with significantly higher leptin concentration and lower adiponectin level. One of the most significant adipokines is resistin, which primarily regulates inflammation and insulin sensitivity. But in recent years, research on resistin has become more and more popular as it has been demonstrated that obesity and obesity-related diseases like diabetes, cardiovascular disease, and cancer are significantly correlated with high levels of resistin **(Rompou *et al.,* 2024).**

Previous hormones are improved by treatment with extracts from red pepper and snake melon seeds. These outcomes are comparable to those reported by **Seyithanoğlu *et al.,* (2016)**, **Wang *et al.,* (2022) and Oh *et al.,* (2023)** who found that feeding rats on diet containing capsaicin reduced liver fat storage and levels of the adipose tissue hormone leptin. Capsaicinoids upregulate adiponectin and other adipokines and inhibit the activity of the enzymes responsible for producing fat in adipose tissue **(Lu *et al.,* 2018 ; Oh *et al.,* 2023 ; Zhang *et al.,* 2024).** Additionally, cucumbers like snake melons are high in phenolic acids like gallic acid, which are the main building blocks for managing obesity because of their ability to suppress appetite, lower cholesterol, inhibit pancreatic lipase, and prevent adipogenesis **(Jamal et al., 2022; Behera et al., 2023) .** Gallic acid is good for energy homeostasis **(Dludla et al., 2018).**

Also, Cucurbits such as snake melon , like most vegetables, are a rich source of dietary fiber (**Rolnik and Olas, 2020).** Long-term use of dietary fiber has been shown to lower serum leptin levels, but only in obese individuals**(Hassanzadeh-Rostami 2021).** According to **Janiszewska *et al.,* (2021),** dietary fiber is a component of food that positively affects adiponectin concentrations. Higher adiponectin concentrations were linked to increased fiber intake, which includes fruit and vegetables .

Table (3) :Effect of red pepper and snake melon seeds extracts leptin , adiponectin , resistin and ghrelin hormones

Groups	Leptin (ng/ml)		Adiponectin (ng/ml)		Resistin (ng/ml)		Ghrelin (ng/ml)	
	Mean ± SD	change%	Mean ± SD	change%	Mean ± SD	change%	Mean ± SD	change%
G1	1.59 ± 0.37^{f}	-----	4.17 ± 0.65^{a}	-----	3.65±0.643^{c}	------	203.2 ± 1.75^{a}	-----
G2	33.08 ± 2.66^{a}	1980.5	0.716 ± 0.18^{c}	-82.82	7.08± 0.951^{a}	93.97	43.35 ± 2.13^{f}	-83.09
G3	11.59 ± 1.75^{d}	-64.96	2.26± 0.20^{b}	215.64	4.66±1.356^{abc}	-34.18	173.03±1.68^{c}	299.14
G4	24.21 ± 1.81^{b}	-26.81	0.833 ±0.15^{c}	16.34	6.4± 1.571^{ab}	-9.60	85.13±1.45^{e}	96.37
G5	5.2 ± 1.41^{e}	-84.28	3.73 ± 0.64^{a}	420.94	3.93±0.550^{bc}	-44.49	192.3±2.33^{b}	343.59
G6	16.60 ± 2.19^{c}	-49.81	1.13 ± 0.32^{c}	57.82	5.33±0.802^{abc}	-24.71	102.7±1.60^{d}	136.90
LSD	3.281	-----	0.740	----	1.86	-----	3.294	

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different (p≤ 0.05). Detailing the numbers for the groups as shown under **Table (2).**

3.4. Effect of red pepper and snake melon seeds extracts on glucose level , insulin and HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) of obese rats

The effect of red pepper and snake melon seeds extracts on glucose level , insulin and HOMA-IR of obese rats is displayed in Table 4. The model group had higher values of glucose level (65.10%), insulin (306.84%), and HOMA-IR (590.60%) compared to normal rats.

Rats fed on red pepper and snake melon seeds extracts (250 and 500 mg/ kg BW) for 28 days had significantly (p ≤ 0.05) lower glucose level, insulin and HOMA-IR by -16.26 , -59.70 and - 67.27% , -30, -71.15 and -80.42 %, -8.83, -6.91 and -16.97% and -13.87, -38.80 and -47.70%, respectively compared to model group. The groups treated with the highest concentration of pepper seeds recorded the best results compared to snake melon seeds groups.

These findings corroborated those of **Xu *et al.*, (2017),** who found that elevated levels of GGT and ALT enzymes in obesity lead to metabolic problems like increased fasting blood glucose and insulin resistance. The relationship between serum liver enzyme levels and obesity provides evidence of a possible mechanism by which obesity contributes to the risk of numerous diseases, including diabetes **(Jalili *et al.*, 2022).** Liver enzymes play a role in the body's metabolism **(Boregowda *et al.*, 2020 and Chen *et al.*, 2021) .** Additionally, obesity is firmly thought to cause diabetes mellitus , with malfunction of the liver, skeletal muscles, and adipose tissue being major contributors according to **Chandrasekaran and Weiskirchen (2024).**

After 28 days of intervention with extracts from red pepper and snake melon seeds (250 and 500 mg/ kg BW), there was a significant reduction in insulin, HOMA-IR, and glucose levels. These findings are in line with the findings of **Varghese *et al.*, (2017),** who highlighted that capsaicinoids enhanced insulin production, supporting weight management and having favorable effects on the prevention and treatment of obesity.They can be utilized to prevent and cure oxidative stress-related disorders like diabetes because of their anti-inflammatory and antioxidant activities **(Uarrota *et al.*, 2021; Gupta *et al.*, 2022 and Xia *et al.*, 2023)**. Red papper seeds (RPS) had a direct and significant inhibitory effect on obesity and insulin resistance in mice fed a high-fat diet, according to research by **Kim *et al.*, (2020a).** The mechanism underlying RPSE's anti-diabetic actions was highlighted by an increase in the phosphorylation of AMP-activated protein kinase (AMPK) and forkhead box protein O1 (FOXO1). Through the activation of FOXO1 and AMPK in obese and diabetic mice, RPSE has the ability to suppress hepatic gluconeogenesis and enhance glycemic control **(Kim *et al.*, 2020b).**

The presence of phytoconstituent may be the cause of the antihyperglycemic effects when snake melon seeds are continuously administered at greater doses, which decreased blood glucose and boosted insulin secretion in the diabetic group **(Sayyar *et al.*, 2023).** Phytoconstituents such as flavonoids, tannins, and polyphenols have been shown to decrease blood glucose absorption in the small intestine, increase peripheral tissue glucose uptake, and enhance glycolysis and glycogen synthase **(Govindarajan *et al.*, 2021).** Previous phytochemical studies have demonstrated that the snake melon seed extract has a high concentration of flavonoids, alkaloids, saponins, phenols, and tannins that produce antioxidant and cytoprotective qualities **(Sereno *et al.*, 2022)** , These compounds may be the cause of blood sugar reductions.

Table (4) : Effect of red pepper and snake melon seeds extracts on fasting blood glucose , insulin and HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) of obese rats

Groups	FBG (mg/dl)		Insulin (µIU/ml)		HOMA-IR	
	Mean ± SD	change%	Mean ± SD	change%	Mean ± SD	change%
G1	101 ± 2.64^{f}	---	3.8 ± 0.26^{c}	-----	0.947±0.080^{e}	-----
G2	166.76 ± 1.62^{a}	65.10	15.46 ± 0.55^{a}	306.84	6.54± 0.375^{a}	590.60
G3	139.63 ± 1.58^{d}	-16.26	6.23± 1 .123^{c}	- 59.70	2.14± 0.394^{d}	-67.27
G4	152.03 ± 2.45^{b}	-8.83	14.46 ± 2.28^{a}	-6.91	5.43± 0.936^{b}	-16.97
G5	116.73 ± 1.27^{e}	-30	4.46 ± 0.550^{c}	-71.15	1.28±0.15^{e}	-80.42
G6	143.63± 1.66^{c}	-13.87	9.46 ± 0.896^{b}	-38.80	3.42±0.295^{c}	-47.70
LSD	**3.451**	**-----**	**2.047**	**----**	**0.824**	**-----**

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different ($p\leq 0.05$). FBG, Fasting blood glucose ; HOMA-IR , Homeostatic Model Assessment for Insulin Resistance). Detailing the numbers for the groups as shown under **Table (2)**.

3.5. Effect of red pepper and snake melon seeds extracts on lipid profiles (TC, TG, HDL and LDL) of obese rats

Table 5 showed the effect of snake melon and red pepper seeds extract on snake melon and red pepper seeds extract on lipid profiles (TC, TG, , HDL and LDL) of obese rats. The obese group had higher values of total cholesterol (267.7%), triglycerides (146.07%) and low-density lipoprotein (1266.13%) compared to the healthy group. As for high density lipoprotein, its level took the opposite direction, as it increased in the healthy group compared to obese group. Feeding rats on pepper and snake melon seeds extracts reduced the level of TG , TC and LDL , while increasing the level of HDL. The pepper seeds groups at different concentrations recorded the best results compared to the snake melon groups.

These findings corroborated those of **Vekic *et al.*, (2023),** who demonstrated that hypertriglyceridemia, a reduction in HDL cholesterol, and a rise in LDL particles are among the lipid abnormalities seen in obese patients. Increased hepatic synthesis of VLDL particles and decreased clearance of TG-rich lipoproteins are the causes of the rise in serum TG. Serum TG levels rise in correlation with generally low HDL-

C levels. While tiny dense LDL is increasing, LDL-C values are often within acceptable limits or only slightly increased.

The effective results of red pepper seeds may be due to capsaicinoids; they stimulate the oxidation and combustion of fat by heat dissipation rather than their sparing in adipose tissue. They also promote the conversion of white adipose tissue to brown **(Silvester *et al.*, 2019 and Irandoost *et al.*, 2021).** Additionally, they diminish the size of adipocytes and stimulate the oxidation of fat and carbohydrates **(Mosqueda-Solis *et al.*, 2018 and Irandoos *et al.*, 2021).** Furthermore, according to **Wang *et al.*, (2021),** capsaicin reduces lipid levels by modifying gut microbiota and intestinal permeability, which in turn affects the gut-brain axis. The information at hand shows that capsaicin and pepper extract can both improve human health and treat a variety of illnesses. Additionally, they can decrease fat storage, which impacts the brain regions in charge of appetite, the gastrointestinal tract's absorption of nutrients, the condition of adipocytes, the oxidation of fat and carbohydrates, metabolism, and thermogenesis, among other processes. Thus, these compounds may prove beneficial in the treatment of obesity, even with certain potential drawbacks **(Sirotkin, 2023).**

Additionally, the extract from snake melon seeds dramatically reduced the triglyceride and total cholesterol levels in diabetic rats. The effects of the cucumis flexuosus seeds extract may be attributed to the rich amounts of phytoconstituents like flavonoids and triterpenoids, which have antioxidant and free radical scavenging properties **(Sayyar *et al.*, 2023)**

Table (5): Effect of red pepper and snake melon seeds extracts on lipid profiles (TC, TG, LDL and HDL) of obese rats

Groups	TC (mg/dl)		TG (mg/dl)		HDL (mg/dl)		LDL (mg/dl)	
	Mean ± SD	Change %	Mean ± SD	Change %	Mean ± SD	Change %	Mean ± SD	Change %
G1	84.06 ± 1.16[f]	----	67.46 ± 1.98[f]	----	53.05±1.97[a]	----	17.51±0.246[f]	------
G2	309.15±1.82[a]	267.7	166 ± 1[a]	146.07	36.73± 1.27[e]	-30.76	239.21±0.548[a]	1266.13
G3	138.18±2.27[d]	-55.30	103± 2[d]	-37.95	45.66± 1.55[c]	24.31	71.91±2.526[d]	-69.93
G4	282.93±2.43[b]	-8.48	141.03±2.15[b]	-15.04	38.03± 1.15[e]	3.53	216.69±0.956[b]	-9.41
G5	117.36±2.03[e]	-62.03	92. 7 ± 1.60[e]	-44.15	48.63±1.60[b]	32.39	50.18±2.72[e]	-79.02
G6	233.47±2.77[c]	-24.48	126.63±1.33[c]	-23.71	41.46±1.97[d]	12.87	166.67±1.066[c]	-30.32
LSD	**3.819**	**-----**	**3.075**	**----**	**2.88**	**-----**	**2.935**	

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different ($p \leq 0.05$).). TC, Total Cholesterol; TG, Triglyceride; HDL, High density lipoprotein; F.A.A, Free Fatty Acid ; LDL,Low density lipoprotein. Detailing the numbers for the groups as shown under **Table (2).**

3.6. Effect of red pepper and snake melon seeds extracts on Thiobarbituric acid reactive substances (TBARS), total antioxidant status (TAS) and Lipid peroxidation (LPO) of obese rats

Table 6 shows the effects of red pepper and snake melon seeds extracts on thiobarbituric acid reactive substances (TBARS) , total antioxidant status (TAS) and lipid peroxidation (LPO) of obese rats. In comparison to the normal group, obese rats exhibited a substantial ($p \leq 0.05$) decrease in TAS (- 42.78%) , as well as a significant increase in TBARS (125%) and LPO (327.21%). On the other hand, after consuming red pepper and snake melon seeds extracts for 28 days, obese rats had significant ($p \leq 0.05$) increases in their TAS values in contrast to the model group. Also, when obese rats treated with red pepper and snake melon seeds extracts, their TBARS and LPO values were considerably ($p \leq 0.05$) lower than those of the model group. The pepper seeds groups at different concentrations recorded the best results compared to the snake melon groups. The best result was achieved by group 5.

Total antioxidant status (TAS) is one of the elements of antioxidant defense mechanisms, whereas thiobarbituric acid reactive substances (TBARS) is a lipid peroxidation index and one of the significant indicators of oxygen reactive species (ROS) activities and is linked to membrane lipid degradation **(Ottaviano et al., 2008).** The generation of free radicals during oxidative assaults alters the cellular dimension's architecture and causes aberrant alterations in macromolecules. Numerous diseases have their own pathophysiology attributed to these harmful alterations. An imbalance favoring prooxidant levels over antioxidant levels leads to oxidative stress. It is a hazardous condition for the body as a whole and manifests symptoms of human illnesses as obesity and cancer **(Olarewaju *et al.*, 2021).**

Research indicated that taking dietary supplements containing capsaicin may help prevent oxidative stress, **Ertekin and Keçeci (2022)** examined the impact of capsaicin on rat TBARS and TAS levels and found that applying capsaicin is only partly effective in preserving the oxidant/antioxidant balance. The therapeutic effects of capsaicin have been linked to several processes, including antioxidation, analgesia, and apoptosis promotion. While the capsaicin receptor (transient receptor potential cation channel subfamily V member 1) is thought to mediate some of the mechanisms, other mechanisms are thought to operate independently of the receptor. Capsaicin's short half-life restricts its clinical utility **(Zhang *et al.*, 2024**).

Also, Carotenoids, which boost food's nutritional value and safety because of their antioxidant activity, are abundant in most vegetables in the *Cucurbitaceae* family **(Yiblet, 2023).** Because of its phytochemical content and nutritious mineral makeup, snake melon has been shown to be a potent antioxidant **(Ilahy *et al.*, 2022).** This suggests that the crop will become even more significant in the near future.

Table (6): Effect of red pepper and snake melon seeds extracts on Thiobarbituric acid reactive substances (TBARS) , total antioxidant status (TAS) and LPO of obese rats

Groups	TBARS (nmol/mL)		LPO (nmol-ml)		TAS (mmol/L)	
	Mean ± SD	change%	Mean ± SD	change%	Mean ± SD	change%
G1	3.2 ± 0.75[c]	----	3.16 ±0.76[d]	-----	15.03 ± 1.1[a]	-----
G2	7.20 ± 1.07[a]	125	13.5 ± 1.32[a]	327.21	8.60 ± 1.7[d]	-42.78
G3	5.26 ±0.75[abc]	-26.94	6.5± 1.32[c]	-51.85	11.8 ± 1.47[bc]	37.20
G4	6.53 ±0.90[a]	-9.30	11.16 ± 1.25[b]	-17.33	9.16 ± 0. 94[cd]	6.51
G5	3.76 ± 0.80[bc]	-47.77	4.8 ± 1.08[cd]	-64.44	13.6 ± 1.01[ab]	58.13
G6	5.76± 1.40[ab]	-20	9.16± 1.04[b]	-32.14	10.8 ± 1.17[cd]	25.58
LSD	**1.73**	**-----**	**2.04**	**-----**	**2.25**	**----**

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different (p≤ 0.05).). TBARS, Thiobarbituric acid reactive substances; LPO, Lipid peroxidation ; TAS, total antioxidant status. Detailing the numbers for the groups as shown under**Table (2).**

3.7. Effect of red pepper and snake melon seeds extracts on thyroid hormones of obese rats

Table 7 shows the effects of red pepper and snake melon seeds extracts on thyroid hormones (T3, T4 and TSH) of obese rats. In comparison to the normal group, obese rats exhibited a substantial (p ≤ 0.05) decrease in T3 (--29.60%) and T4(-67.64%) as well as a significant increase in TSH (1295%). On the other hand, after consuming red pepper and snake melon seeds extracts for 28 days, obese rats had significant (p≤0.05) increases in their T3 and T4 values in contrast to the obese group. Also, when obese rats treated with red pepper and snake melon seeds extracts for 28 days, their TSH values were considerably (p≤0.05) lower than those of the model group. Red pepper groups achieved better results than snake melon groups.

These findings are completely consistent with those of **Biondi (2023),** who investigates the relationship between obesity and subclinical hypothyroidism. A condition known as subclinical hypothyroidism (SHypo) occurs when free thyroid hormone levels fall below the lower bound of their normal reference range. This early stage of thyroid hormone deficiency elevates serum thyroid-stimulating hormone (TSH), which is already beyond its recommended limit **(Biondi and Cappola 2022).** Because hypothyroidism is linked to lower resting energy expenditure and thermogenesis, there is a strong correlation between obesity and hypothyroidism **(Duntas *et al.*, 2013).** According to **Kochman *et al.*, (2021),** hypothyroidism causes oxidative damage and altered lipid metabolism in thyroid cells by reducing antioxidant system function, which in turn promotes oxidative stress. The protective impact of nutritional antioxidants against oxidative stress in thyroid disorders is studied by **Macvanin *et al.*, (2023) .** For this reason, the efficiency of both pepper and snake melon seeds in improving thyroid hormone levels in obese rats could be explained by their high level of naturally occurring antioxidants.

Table (7) : Effect of red pepper and snake melon seeds extracts on thyroid hormones of obese rats

Groups	T3 (ng/ ml)		T4(ng/ ml)		TSH (mg/ dl)	
	Mean ± SD	change%	Mean ± SD	change%	Mean ± SD	change%
G1	80.16 ± 1.25[a]	----	3.4 ± 0.5[a]	-----	0.124 ±0.021[e]	------
G2	56.43 ± 1.55[e]	-29.60	1.1 ± 0.1[b]	-67.64	1.73 ±0.09[a]	1295
G3	70.2 ±0.95[c]	24.40	2.06± 0.208[b]	87.27	0.82 ± 0.11[c]	-52.60
G4	58.5 ± 2.29[e]	3.66	1.3 ± 0.2[b]	18.18	1.5 ±0.1[b]	-13.29
G5	75.6 ± 1.12[b]	33.97	3.2 ± 0.75[a]	190.9	0.32 ±0.11[d]	-81.50
G6	63.13± 1.88[d]	11.87	1.76± 0.25[b]	60	1.33 ±0.152[b]	-23.12
LSD	2.80	-----	0.717	----	0.186	-----

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different ($p \leq 0.05$). T3, Triiodothyronine; T4, Thyroxine; TSH , Thyroid-stimulating hormone. Detailing the numbers for the groups as shown under **Table (2).**

3.8. Effect of red pepper and snake melon seeds extracts on cardiac Troponin I, Troponin T, CK-MB and myoglobin of obese rats

Table 8 shows the effect of red pepper and snake melon seeds extracts on cardiac Troponin I , Troponin T , CK-MB and myoglobin of obese rats. Rats fed on high fat diet had significantly ($p \leq 0.05$) higher levels of Troponin I (2400%), Troponin T (800%), CK-MB(314.9) and myoglobin (57.43%) in comparison to normal rats. By contrast, feeding rats on red pepper and snake melon seeds extracts reduced the level of myoglobin , CK-MB , cardiac Troponin I and Troponin T of obese rats. The pepper seeds groups at different concentrations recorded the best results compared to the snake melon groups.

The findings align with the findings of **Welsh *et al.*, (2024),** who noted that obesity significantly increases the chance of developing established risk factors for cardiovascular disease, including dyslipidemia, diabetes, hypertension, and chronic renal disease. A high-fat diet's induction of elevated blood lipid levels is thought to play a significant role in CVD **(Wali *et al.*, 2020).** Increases in pulmonary artery pressure and intracardiac filling pressure are two further detrimental effects of fat. Over time, obesity-related structural and hemodynamic changes can make a person more susceptible to systolic and diastolic heart failure. Obesity-related heart failure is primarily caused by a cascade of metabolic dysfunction and disease states, moreover to the direct impact of obesity on the anatomy and functionality of the heart **(Gadde *et al.*, 2018).**

Atherosclerosis, cardiomyopathy, hypertension, and stroke can all be treated with capsaicin. Through an independent and TRPV1-dependent mechanism, it prevents platelet aggregation. Capsaicin increases platelet activation via improving ADP and calcium release from cellular platelet stores mediated by thrombin. Capsaicin reduces LDL-related protein 1 and increases ATP-binding cassette transporter A1, which limits atherosclerosis. The heart has capsaicin-sensitive nerves. Through activation of TRPV1 and substance P, these neurons control the release of the peptide associated with the calcitonin gene. Capsaicin causes vasodilation by causing vascular endothelial cells to release nitric oxide. Via blocking vascular smooth muscle's L-type calcium channels, it also has antihypertensive effects **(Nandagopal and Nemala, 2024).**

Therefore, the research results showed a positive effect of red pepper seeds on improving heart enzymes.The anti-oxidative, anti-inflammatory, and radioprotective qualities of GA in snake melon seeds are linked to possible health advantages **(Ferk et al., 2018).** According to a number of studies, Gallic acid may help treat cardiovascular conditions such as vascular calcification, myocardial dysfunction brought on by diabetes, and cardiac hypertrophy and fibrosis brought on by isoproterenol **(Ryu et al., 2016).** Additionally, recent research has shown that GA prevents cardiac remodeling, l-NAME (Nω-nitro-larginine methyl ester hydrochloride)-induced hypertension, and myocardial fibrosis brought on by pressure overload **(Yan et al., 2019)**. Furthermore, gallic acid has been shown by **Jin et al. (2018)** to be a promising new therapeutic agent for the treatment of heart failure fibrosis and cardiac dysfunction.

Also**, Fu *et al.*, (2022)** investigate the potential benefits of dietary fiber supplementation on recognized cardiovascular risk factors. Given that snake melon seeds are an excellent source of GA and dietary fiber, this helps to explain their beneficial effect on lowering cardiac enzymes.

Table (8) : Effect of red pepper and snake melon seeds extracts on cardiac Troponin I , Troponin T , CK-MB and myoglobin of obese rats

Groups	Troponin I (ng / ml)		Troponin T (ng / ml)		CK-MB (U/L)		Myoglobin (ng / ml)	
	Mean ± SD	change %	Mean ± SD	change%	Mean ± SD	change %	Mean ± SD	change%
G1	0.02 ± 0.005[c]	----	0.01 ±0.008[c]	-----	6.7 ± 1.21[e]	------	53.1±0.95[e]	------
G2	0.5 ± 0.1[a]	2400	0.09 ± 0.01[a]	800	27.8 ± 1.08[a]	314.92	83.6 ±1.46[a]	57.43
G3	0.07 ± 0.015[c]	-86	0.04± 0.01[b]	-55.55	17.06 ± 1.61[c]	-38.63	64.6± 1.34[c]	-22.72
G4	0.42 ± 0.105[a]	-16	0.08 ±0.02[a]	-11.11	27.46 ±1.02[a]	-1.22	82.2±1.1[a]	-1.67
G5	0.03 ± 0.01[c]	-94	0.02 ±0.01[bc]	-77.77	11.16 ± 1.75[d]	-59.85	57.33±1.56[d]	-31.42
G6	0.22± 0.10[b]	- 56	0.07± 0.01[a]	-22.22	22.76 ± 1.98[b]	-18.12	72.36±1.95[b]	-13.44
LSD	**0.128**	**-----**	**0.021**	**----**	**2.65**	**-----**	**2..55**	**-----**

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different (p≤ 0.05). CK-MB, Creatine Kinase-MB. Detailing the numbers for the groups as shown under **Table (2)**.

3.9. Effect of red pepper and snake melon seeds extracts on liver enzymes of obese rats

Table 9 shows the effect of snake melon and red pepper seeds extract on liver enzymes of obese rats. It is noted from the table that liver enzymes increased in the obese group fed a high-fat diet compared to the healthy group .Giving obese rats extracts of both pepper seeds and snake melon seeds reduced the level of liver enzymes compared to model group, The most favorable outcomes were noted for the pepper seeds groups compared to the snake melon seeds groups. These findings corroborated those of **El-Eshmawy (2023)** , who demonstrated that abnormal liver function tests (LFT) in obesity were linked to raised blood levels of transaminases and reduced albumin and bilirubin levels in the blood . Oxidative damage, insulin resistance and inflammation are some of the additional underlying factors contributing to the aberrant LFT observed in obesity.

Pretreatment with capsaicin shields mice's livers from damage caused by Con A. It also has a role in controlling the activation and recruitment of intrahepatic leukocytes, as well as reducing oxidative stress, inflammatory mediators, and hepatocyte apoptosis **(Zhang *et al.*, 2019).** Furthermore, red pepper seeds prevent the buildup of hepatic lipids by triggering autophagy through AMP-activated protein kinase (AMPK) activation, according to research by **Lee *et al.*, (2022).** By reducing apoptosis and mitochondrial dysfunction, capsaicin guards against septic acute liver injury **(Ghorbanpour *et al.*, 2023).**Capsaicin (CPS) reduces the hepatotoxicity caused by cyclophosphamide (CPM) by modifying the cytokine pathway, apoptotic signals, and oxidative stress. As such, CPS may be useful as an adjuvant for patients receiving chemotherapy **(Alam *et al.*, 2023).**

Flavonoids, triterpenoids, phenolic compounds, and anthraquinine are among the phytoconstituents that have been shown to have hepatoprotective properties **(Domitrović& Potočnjak, 2016).** According to **Sayyar *et al.*, (2023),** administering extract of snake melon seeds for 30 days resulted in the regulation and normalization of liver enzymes, further supporting the extract's antidiabetogenic activity. The effects of the snake melon seeds extract could be explained by the existence of phytoconstituents like flavonoids and triterpenoids, which are present in rich amounts.

Table (9) : Effect of red pepper and snake melon seeds extracts on liver enzymes of obese rats

Groups	ALT (U/ L)		AST(U/ L)		ALP (U/ L)	
	Mean ± SD	change%	Mean ± SD	change%	Mean ± SD	change%
G1	27.8 ± 2.17^{e}	----	66.73 ± 1.19^{f}	-----	152.86±2.44^{f}	------
G2	90.96 ± 1.79^{a}	227.19	162.76 ± 1.56^{a}	143.90	413.46 ±2.21^{a}	170.48
G3	43.4 ± 1.60^{d}	-52.28	87.66± 2.51^{d}	-46.14	186.9± 1.87^{d}	-54.79
G4	71.12 ± 1.94^{b}	-21.81	142.2 ± 1.9^{b}	-12.63	308±2^{b}	-25.50
G5	30.4 ± 1.67^{e}	-66.57	72.63 ± 1.02^{e}	-55.37	161.73±1.40^{e}	-60.88
G6	54± 1.15^{c}	-40.63	120.26± 1.95^{c}	-26.11	252.46±2.35^{c}	-38.93
LSD	**3.11**	**-----**	**3.138**	**----**	**3.96**	**-----**

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different ($p \leq 0.05$). ALT, Alanine transaminase; AST, Aspartate transferase; ALT, alkaline phosphatase. Detailing the numbers for the groups as shown under **Table (2).**

4. Conclusion

Oral administration of red pepper and snake melon seeds ethanolic extracts showed reliable anti-obesity potential to increase metabolism through two possible mechanisms, lipid-lowering effect and TSH activation. Moreover, the decline of TBARS concentration confirmed the free radical defensive function of red pepper and snake melon seeds ethanolic extracts by increasing total antioxidant status which helped to reduce obesity complications.The results obtained encourage further research in this point to ascertain the appropriate dosage and provide novel theories for the mechanisms of the useful characteristics of red pepper and snake melon seeds that may be reached. Therefore, the research results recommended including both red pepper and snake melon seeds at concentrations up to (500 mg/kg body weight) in our daily diets, beverages and nutritional supplements.

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التأثيرات المحتملة للمستخلصات الإيثانولية لبذور الفلفل الأحمر الحار وبذور القثاء على السمنة ومضاعفاتها الناجمة عن النظام الغذائي الغني بالدهون في الفئران : دراسة مقارنة

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ملخص البحث

السمنة هي حالة مزمنة تؤثر على أكثر من ثلث سكان العالم وتسبب عبئًا على صحة الإنسان في كل من البلدان المتقدمة والنامية. وفي الوقت الحالي، هناك حاجة متزايدة إلى علاجات طبيعية فعالة للسمنة . لقد حظيت بذور النباتات باهتمام كبير مؤخرًا بسبب كفاءتها وتوافقها البيولوجي. لذلك، كان الغرض من هذه الدراسة هو معرفة التأثيرات المحتملة لمستخلص بذور الفلفل الأحمر ومستخلص بذور القثاء على السمنة ومضاعفاتها في الفئران . من خلال تحليل المكونات النشطة بيولوجيًا في مستخلص بذور الفلفل الأحمرومستخلص بذور القثاء ، وجد أن في مستخلص بذور الفلفل الأحمر يحتوي على تركيزات أعلى من المركبات الفينولية النشطة. من ناحية أخرى، أشارت التجربة البيولوجية إلى أن تغذية الفئران الطبيعية بنظام غذائي عالي الدهون لمدة 4 أسابيع (نموذج التحكم) أدى إلى زيادة كبيرة في وزن الجسم ، والمأخوذ من الطعام، ومعدل الاستفادة من الغذاء عند مقارنتها بالمجموعة الطبيعية. ومع ذلك، بعد أربعة أسابيع من تغذية الفئران البدينة على تركيزات 250 و 500 مجم / كجم من وزن الجسم من كل من مستخلص بذور الفلفل الأحمرومستخلص بذور القثاء ، تحسنت معايير صورة الدهون في المصل بشكل كبير. كما تحسنت وظائف الكبد، والإنزيمات القلبية (تروبونين، الكرياتين كيناز، الميوجلوبين)، وهرمونات الغدة الدرقية (هرمون ثلاثي يودوثيرونين، الثيروكسين، الهرمون المحفز للغدة الدرقية)، ومستويات اختبار المادة التفاعلية مع حمض الثيوباربيتيوريك، وبيروكسيد الدهون ، وحالة مضادات الأكسدة الكلية، والمؤشرات الحيوية لمرض السكري (تحليل الجلوكوز أثناء الصيام، مقاومة الانسولين، مستويات الأنسولين)، وهرمونات الشبع والجوع (اللبتين، الجريلين)، ومستويات هرمون الأديبونيكتين والريزيستين في البلازما عند مقارنتهما بمجموعة النموذج . وكان تأثير مستخلص بذور الفلفل الأحمر على العلامات السابقة أفضل من تأثير مستخلص بذور القثاء، لذلك توصي هذه الدراسة بإمكانية إضافة بذور الفلفل الأحمر إلى المكملات الغذائية للوقاية من السمنة ومضاعفاتها.

الكلمات المفتاحية: الأديبوكينات، المؤشرات الحيوية للقلب، مقاومة الانسولين ، بيروكسيد الدهون، القثاء ، الفلفل الأحمر الحار.