Trop J Nat Prod Res, November 2025; 9(11): 5420 - 5426 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Preventive Effect of Mandarin Peel on Dyslipidemia and Hyperglycemia Associated with Obesity Induced by Cafeteria Diet

Tawfik Addi*, Soumia Fenni, Fatma Z. Ameur, Amira S. Omari, Bouchra I. Cherrak, Samia Addou

[1]*Department of Biology, Faculty of Natural and Life Sciences, Laboratory of Nutrition Physiology and Food Safety, University Oran 1 Ahmed Benbella, B.P 1524 El M'Naouer, 31000 Oran, Algeria*

ARTICLE INFO

Article history:
Received 09 October 2025
Revised 30 October 2025
Accepted 11 November 2025
Published online 01 December 2025

ABSTRACT

Obesity is an emerging health problem, characterized by dyslipidemia, hyperglycemia, and cardiovascular risk. Mandarin (*citrus reticulata*) peel (MP) is used in traditional chinese medicine. Its bioactive compounds, including flavonoids, vitamins, and carotenoids, may help prevent obesity. In this study, we evaluated the effects of MP from western Algeria on obesity and related metabolic parameters in mice. Forty mice were divided into five groups of eight, and were fed different diets for eleven weeks : standard diet, cafeteria diet, cafeteria diet supplemented with 5% and 10% MP powder, cafeteria diet supplemented with MP infusion [5g MP/250ml water] administered orally *ad libitum*. Body weight was regularly monitored. At the end of 11 weeks, Blood was collected for lipid and glycemic analyses, and the mice were subsequently euthanized. Histological sections of adipose tissue and liver were performed, and hepatic triglycerides were measured. Our results showed that a cafeteria diet supplemented with 5% or 10% MP powder or infusion significantly ($P < 0.05$) reduced body, liver, and adipose tissue weights compared to the cafeteria diet alone. The supplementation with 5% and 10% MP powder significantly ($P < 0.05$) reduced plasma levels of total cholesterol, triglycerides, low-density lipoprotein and glycemia, and increased high-density lipoprotein (HDL) compared to the cafeteria group without supplementation. The MP infusion significantly ($P < 0.05$) reduced triglyceride and increased HDL. Both MP powder and infusion reduced adipocyte hypertrophy and prevented hepatic triglyceride accumulation. These results suggest that MP may help prevent obesity and related metabolic disorders, serving as a phytotherapeutic agent.

Keywords: Obesity, Dyslipidemia, Hyperglycemia, Mandarin peel, Phytotherapy

Introduction

Obesity is a global public health problem. Its worldwide prevalence has increased dramatically and leads to avoidable deaths as well as numerous diseases and complications.[1] Obesity is associated with excessive accumulation of visceral and ectopic fat.[2] This accumulation poses a high risk of cardiovascular morbidity, primarily due to increased chronic inflammation and oxidative stress.[3] Obesity is also manifested by dyslipidemia, characterized by increasing levels of total cholesterol, triglycerides, and low density lipoprotein (LDL) cholesterol, along with low levels of high density lipoprotein (HDL) cholesterol associated with the occurrence of cardiovascular complications such as atherosclerosis, myocardial infarction, and stroke in obese individuals.[4] Obesity is also linked to type 2 diabetes and hypertension, as well as other metabolic issues that increase the risk of complications. Additional risk factors may facilitate the rapid progression of obesity and the emergence of problems, including insufficient physical activity and, crucially, an unhealthy diet.[5] Nutritional choices significantly influence the risk and development of obesity. A diet rich in saturated fats, added sugars, and salt, along with the intake of processed and fast foods, elevates the risk of obesity.[6]

*Corresponding author. Email: addi.tawfik@univ-oran1.dz
Tel.: +213 552 06 79 61

Citation: Addi T, Fenni S, Ameur FZ, Omari AS, Cherrak BI, Addou S. Preventive Effect of Mandarin Peel on Dyslipidemia and Hyperglycemia Associated with Obesity Induced by Cafeteria Diet. Trop J Nat Prod Res. 2025; 9(11): 5420 – 5426 https://doi.org/10.26538/tjnpr/v9i11.23

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

Conversely, balanced meals rich in fruits, vegetables, grains, cereals, and fish are associated with a reduction in obesity and hyperglycemia.[6] These foods, rich in vitamins, minerals, polyphenols, carotenoids, fiber, and omega-3 fatty acids, promote cardiovascular health by reducing inflammation, regulating weight, and improving the lipid profile.[4] The right diet and physical activity are essential for managing obesity but obese individuals often turn to non-natural pharmacological treatments, which can lead to drug-related disorders. Several studies highlight the role of natural products in the prevention of metabolic diseases.[7,8] Thus, encouraging natural phytotherapeutic alternatives is essential for health. The mandarin (*Citrus reticulata*, family *Rutaceae*) is a small citrus species characterized by a thin, easily peelable orange rind and a sweet, aromatic pulp. Mandarins are primarily cultivated in subtropical and Mediterranean regions characterized by mild winters and warm to hot summers, which provide optimal climatic conditions for their growth and fruit development. The peel of Mandarin, also known as chenpi, possesses numerous beneficial properties. It is used as a condiment in Chinese cuisine and also in traditional medicine. Mandarin peel (MP) is rich in fiber and pectin, which can regulate metabolic disorders.[9] It contains an abundance of polyphenols, particularly flavonoids, whose therapeutic effects have been widely described as antioxidant, anti-inflammatory, anti-hyperglycemic, and anti-dyslipidemic.[10–12] Other bioactive compounds are present in mandarin peel, such as carotenoids and vitamins,[10,13] which are beneficial against obesity and its detrimental effects, including type 2 diabetes, hypercholesterolemia, and inflammation.[14,15] Mandarin peel also contains the essential oil limonene, which has proven effects against metabolic disorders.[16] Extraction studies from mandarin peels have shown that extracts rich in bioactive compounds have beneficial effects on insulin resistance, oxidative stress, inflammation, as well as obesity and dyslipidemia.[17,18] Additionally, it has been demonstrated that some flavonoids, such as hesperidin and narirutin found in mandarin peel, have effects on weight gain, fat accumulation, and lipid and glycemic disorders.[19–22] However, the effect of mandarin peel consumed in powder or infusion form on

cafeteria diet-induced obesity remains to be studied. The cafeteria-style diet, rich in calories, fats, sugars, and salts, similar to "Western" or "junk food" diet, serves as a reference dietary model for studying the mechanisms of obesity in animal models.[23] The objective of this study is to examine the preventive effect of mandarin peel (MP) from the western region of Algeria in powder and infusion form on the development of dyslipidemia and obesity induced by a cafeteria diet.

Materials and Methods

Mandarin peel and cafeteria diet preparation

The mandarin (*Citrus reticulata*) was harvested in December 2023 from biological farms in the western region of Algeria, in the city of Mostaganem (Latitude : 35.85° N, Longitude : 0.05° E). It was carefully washed, then the peel was removed and air-dried for five to seven days. The dried peel was then ground into powder using a blender, a part of the powder was infused in distilled water at a ratio of 5 g in 250 ml of boiling water for 20 minutes, and then both the dried powder and infusion were stored in a refrigerator.

The cafeteria diet was prepared according to the recommendations established in litterature.[24] It consists of 50% of the basic diet mixed with 50% of a mixture that includes two portions of hot dog, biscuits (Galette Bimo), and cheese, as well as one portion of chips, chocolate, and sausage. The preparation was then kept cool in a refrigerator below 10°C.

Animal Model and Experimentation

Male Swiss *NMRI* (*Naval Medical Research Institute*) mice (24-26g, 7 weeks old) were obtained from the Pasteur Institute in Algeria and were acclimatized to our laboratory environment for two weeks before the experimental session. They were kept in a room at a controlled temperature of 23 ± 2 °C, with a humidity of 55 ± 10 % under a light/dark cycle of 12 hours, and they were provided with water and food *ad libitum*. The animals (Ethics approval :45/DGLPAG/DVA.SDA.14) were divided into five groups of eight animals. Group ST : received a standard laboratory diet daily, Group CAF : received a cafeteria diet daily, Group CAF+MP5% : received a cafeteria diet supplemented with 5% mandarin peel powder daily, Group CAF+MP10% : received a cafeteria diet supplemented with 10% mandarin peel powder daily, Group CAF+MP INF : received a cafeteria diet daily and mandarin peel infusion twice a week (5g MP infused in 250 ml water, administered orally *ad libitum*, using a ball-tipped drinking bottle). The diets were prepared once a week and stored in opaque bottles at 4°C. Body weight was recorded weekly whereas feed consumption was monitored daily, and the remaining 120ml of the initial infusion volume was measured the following day, during 11 weeks of experiment. This study was approved by the Algerian Institutional Animal Ethics Committee (approval number : 45/DGLPAG/DVA. SDA.14) and supported by the Ministry of Higher Education and Scientific Research - Algeria. The experiments were conducted in accordance with ethical guidelines for the care of animals.

Blood collection and tissue preparation

At the end of the experiment, the mice were fasted overnight, and approximately 1.5 ml of blood was collected via retro-orbital puncture and centrifuged at 3500 rpm for 15 minutes at 4°C. The plasma was separated and stored at -20°C for lipid profile analysis and glycemia determination. After blood collection, the mice were euthanized by cervical dislocation, and their liver, perirenal and epididymal adipose tissue, were immediately removed and weighed. The liver and adipose tissues were preserved in formalin for histological sections or stored at -20°C for the measurement of hepatic triglycerides.

Biochemical analysis

Serum total cholesterol (TC), triglyceride (TG) and High-density lipoprotein (HDL) were determined by enzymatic colorimetric methods,[25] using the BioSystems kit's (21505, 23557, 23528) France. Low-density lipoprotein (LDL) was estimated using the Friedewald equation,[26]: LDL-C = TC - (HDL + TG/5). Fasting blood glucose levels were also measured by enzymatic colorimetric methods,[27] using BioSystems kit's (11803) France. Liver tissues were homogenized in phosphate-buffered saline (PBS) and centrifuged at 3000 rpm for 5 minutes at 4 °C following a standard protocol.[28] Triglyceride (TG) concentrations were measured using an enzymatic colorimetric assay BioSystems kit (23557). Total protein content in the homogenates was determined by the Bradford method,[29] and hepatic TG levels were normalized to protein concentration, expressed as µg of TG per mg of protein.

Histological examination

For histological investigation, liver and epididymal adipose tissue samples were fixed in 10% buffered formalin, embedded in paraffin, and cut into 5 µm sections stained with hematoxylin and eosin (H&E). The images were obtained using a light microscope (Olympus CX22LED, Japan). Image J software was used to measure the area of adipocytes (µm²).

Statistical analysis

The statistical analysis were performed using the Prism (GraphPad Software Inc, CA). Data are expressed as the mean ± SEM for 8 mice. Significant differences between CAF group and ST or MP treated groups were revealed by Student's t-test for values with normal distribution or Mann-Whitney test for non-normally distributed values. Numerical variables were tested for normality by the Shapiro–Wilk test. A p value lower than 0.05 was considered significant.

Results and Discussion

Effect of mandarin peel on weight gain, liver weight and adipose tissue accumulation

The cafeteria diet is a high-fat, high-carbohydrate regimen that effectively induces obesity in mice, closely mimicking human "junk food" consumption.[23] It has been shown that the cafeteria diet induces weight gain and fat accumulation associated with hypercholesterolemia and hyperglycemia.[30] We monitored the weight progression of the mice over the eleven weeks. The mice fed with the CAF diet exhibited a significant increase in their body weight ($P \leq 0.05$) compared to the group on the standard diet (ST) and the groups that received mandarin peel powder or infusion (Figures 1 A and B). Furthermore, mice fed a ST diet, CAF diet, and those that received supplementation with mandarin peel powder or infusion had an average food intake ranging from 50 g to 60 g per day during the week (Figure 1C). It is also interesting to note that there was no difference in average daily food intake over the eleven weeks (Figure 1D). Regarding the mandarin peel infusion, the average consumption for the group of mice was approximately 70 mL per day.

The effect of mandarin peel powder and infusion on the weight of the liver, the perirenal and epididymal adipose tissues was examined. Our results showed that CAF group had a significantly higher ($P < 0.05$) relative and absolute weight of the liver compared to the ST group or the groups supplemented with mandarin peel powder at 5% and 10% or mandarin peel infusion (Figures 2 A and B). On the adipose tissue weight CAF consumption significantly increased ($P < 0.01$) relative and absolute mass perirenal and epidydimal adipose tissue weights compared to the ST group (Figures 2 C.D and E.F). Compared to CAF group, the supplementation with mandarin peel powder at 5% and 10% or mandarin peel infusion significantly decreased ($P < 0.05$ and $P < 0.01$ respectively) the relative and absolute weight of perirenal and epidydimal adipose tissue (Figures 2 C.D and E.F). Our findings indicate that mandarin peel powder and infusion attenuate the effects of the cafeteria diet on liver weight and on perirenal and epididymal adipose tissue weight. Results reported by Qian et al. (2021)[31] also demonstrated that supplementation with mandarin peel originating from China could impact fat accumulation in mice on a normal diet. Another study also demonstrated the preventive effect of a compound extract obtained through an aqueous extraction method from an immature mandarin peel on fat accumulation in mice subjected to a high-fat diet.[32]

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

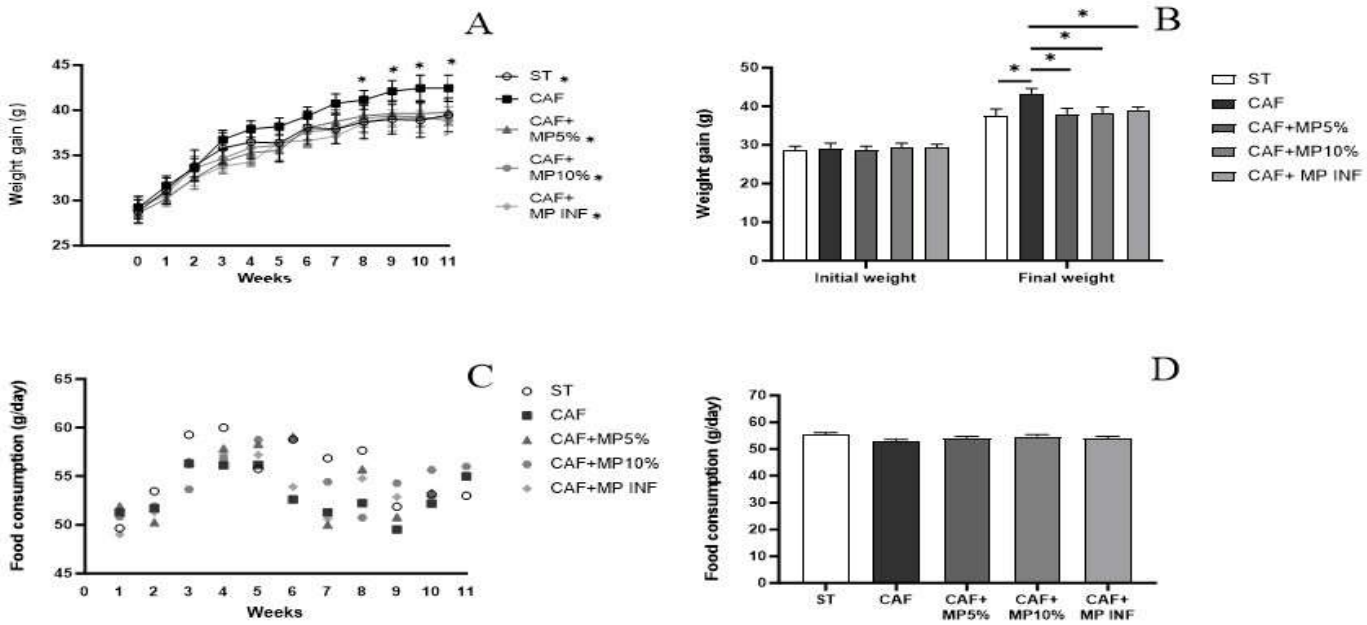

Figure 1: Effect of Mandarin peel on food consumption and weight gain. (A)Weight gain per week. (B) Initial and final weight. (C)Food consumption average per weekday. (D) Food consumption average per day during the eleven weeks. ST : Standard diet, CAF : Cafeteria diet, MP : Mandarin peel, MP INF : MP Infusion. The amount of food ingested is expressed in g/day. Data are expressed as the mean ± SEM (n=8). * $P \leq 0.05$; indicates significant differences compared with the only CAF group

Mandarin peel positively influences lipid parameter and glycemia levels

Dyslipidemia is characterized by an increase in total cholesterol, triglycerides, LDL levels, often associated with a decrease in HDL.[33] These characteristics are directly associated with inflammatory problems, specifically atherosclerosis and other cardiovascular issues, including stroke, myocardial infarction, and venous thrombosis in obese persons.[3] While high levels of HDL may suggest a cardioprotective role.[34] In our study, we evaluated the effect of mandarin peel powder and infusion supplementation on dyslipidemia. As demonstrated in Figure 3, the CAF fed mice had significantly increased levels of total cholesterol (TC) ($P < 0.01$), triglycerides (TG) ($P < 0.01$), and low-density lipoprotein (LDL) ($P < 0.01$) and a significantly decreased level of high-density lipoprotein (HDL) ($P < 0.05$) compared to the ST fed mice (Figure 3). However, 5% and 10% mandarin peel powder supplementation significantly decreased ($P < 0.05$ and $P < 0.01$ and $P < 0.001$) the concentrations of TC, TG, and LDL respectively, while HDL was significantly increased ($P < 0.01$) compared to the CAF group (Figure 3). This finding confirms the efficacy of mandarin peel powder in inhibiting the increases of lipid parameters ; TC, TG, and LDL, while maintaining stable levels of HDL, following a cafeteria diet. Notably, there were no significant variations in our results between the 5% and 10% mandarin peel powder supplementation. Nevertheless, in the group supplemented with mandarin peel infusion, there was no significant difference in TC and LDL levels compared to the CAF group. However, a significant decrease ($P < 0.05$) in TG concentration and a significant increase ($P < 0.05$) in HDL concentration were observed (Figure 3). This indicates that powdered mandarin peel is preferable to an infusion, as the powdered peel exhibits greater efficacy.

Obesity is often associated with hyperglycemia. In our résultats, the glycemia was significantly higher ($P < 0.05$) in the CAF fed mice compared to the ST fed mice. The mandarin peel powder supplementation at 5% and 10% significantly decreased ($P < 0.05$) glycemia levels compared to the CAF group, and non-significantly lower levels were observed in the group supplemented with mandarin peel infusion compared to the CAF group (Figure 3 E). These results validate the preventive effect of mandarin peel powder on hyperglycemia induced by the cafeteria diet. However, supplementation with mandarin peel infusion did not significantly reduce glucose levels in this group. This still buttresses the point that the powder is better than the infusion. Thus, it is possible that administering mandarin peel infusion twice a week in this study was not sufficient to significantly reduce TC, LDL, and glycemia. Consumption more than twice a week may have a better effect. Moreover, the absence of heat treatment could enhance the efficacy of the powdered mandarin peel. On the other hand, the infusion of mandarin peel allows for the extraction of certain active ingredients while eliminating the fibers, whereas it is suggested that citrus peel fibers can reduce hypercholesterolemia and hyperglycemia by modulating lipid metabolism and decreasing glucose absorption.[35] Thus, mandarin peel powder may be more effective as a supplement. In literature, similar results in mice fed a high-fat diet demonstrated that polyphenol-rich mandarin peel extract compound reduce levels of lipid parameters including TC, LDL, and TG, and may stabilize fasting blood glucose levels.[36] Our results also align with some studies describing the potential role of extracts from some types of mandarin or *citrus* peel in reducing lipid and glucose parameter levels in a high-fat diet.[21,37,38] Castro and his team also highlighted the potential role of mandarin peel oil in preventing atherosclerosis through a mechanism that involves inhibiting lipid synthesis and storage, along with reducing lipid peroxidation of LDL.[17] Thus, mandarin peel could serve as an effective agent in preventing the dysregulation of metabolic parameters induced by an obesogenic diet.

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

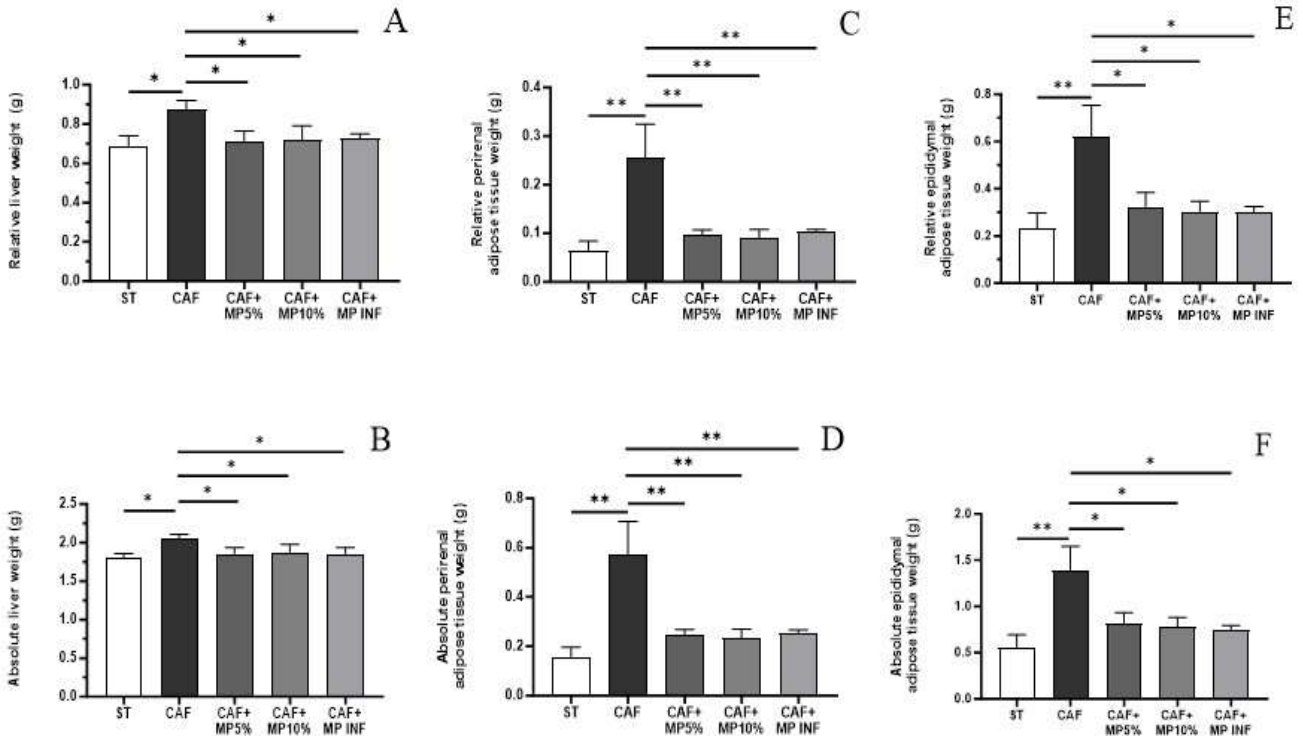

Figure 2: Effect of Mandarin peel on liver weight and adipose tissue accumulation. (A)(B) Relative and absolute liver weight (g). (C) (D) Relative and absolute perirenal adipose tissue weight (g). (E) (F) Relative and absolute epididymal adipose tissue weight (g). ST : Standard diet, CAF : Cafeteria diet, MP : Mandarin peel, MP INF : MP Infusion. The relative weight is determined by the ratio of the liver or adipose tissues weight/total weight of mice × 100. Data are expressed as the mean ± SEM (n=8). * $P \leq 0.05$; ** $P \leq 0.01$; indicates significant differences compared with the only CAF group

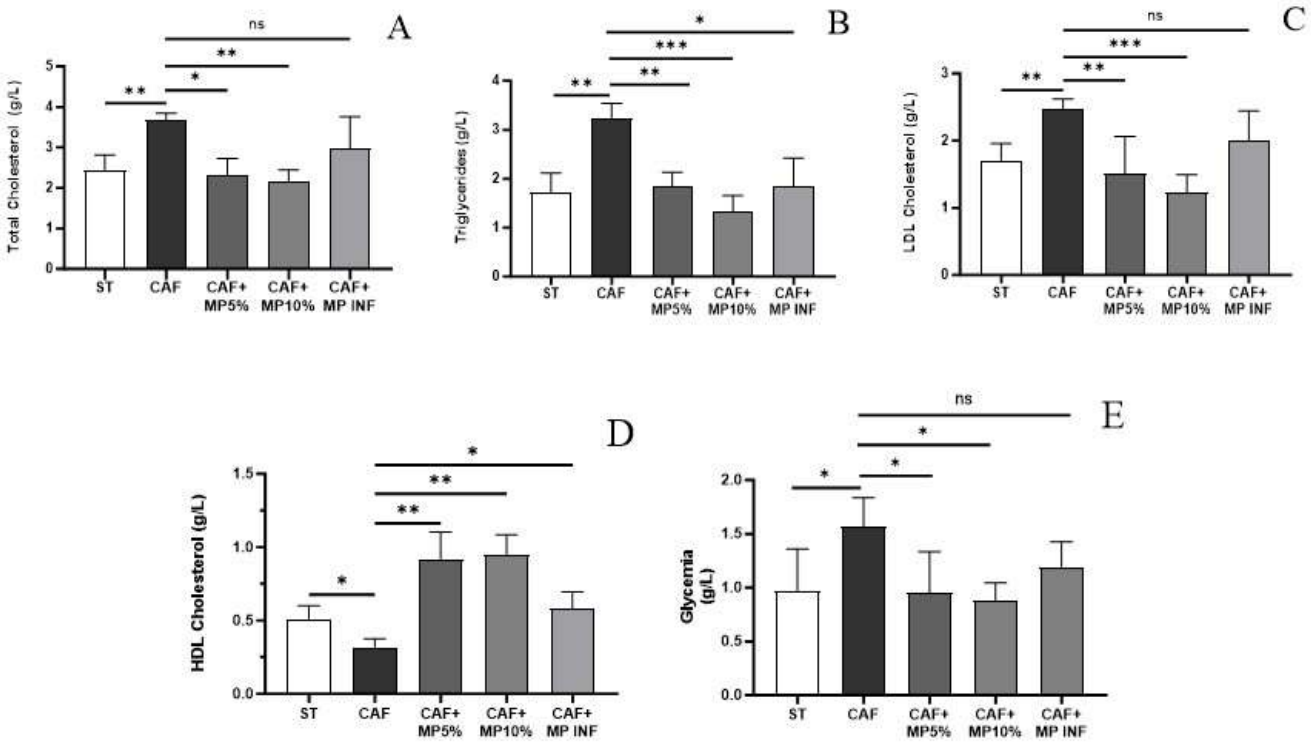

Figure 3: Effect of Mandarin peel on metabolic parameters and glucose homeostasis. (A)Total cholesterol. (B) Triglycerides. (C) LDL cholesterol. (D) HDL cholesterol. (E) Glycemia. ST : Standard diet, CAF : Cafeteria diet, MP : Mandarin peel, MP INF : MP Infusion. Lipid parameter and glycemia measurements were performed using enzymatic colorimetric techniques. Data are expressed as the mean ± SEM (n=8). * $P \leq 0.05$; ** $P \leq 0.01$; *** $P \leq 0.001$ indicates significant differences compared with the only CAF group

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

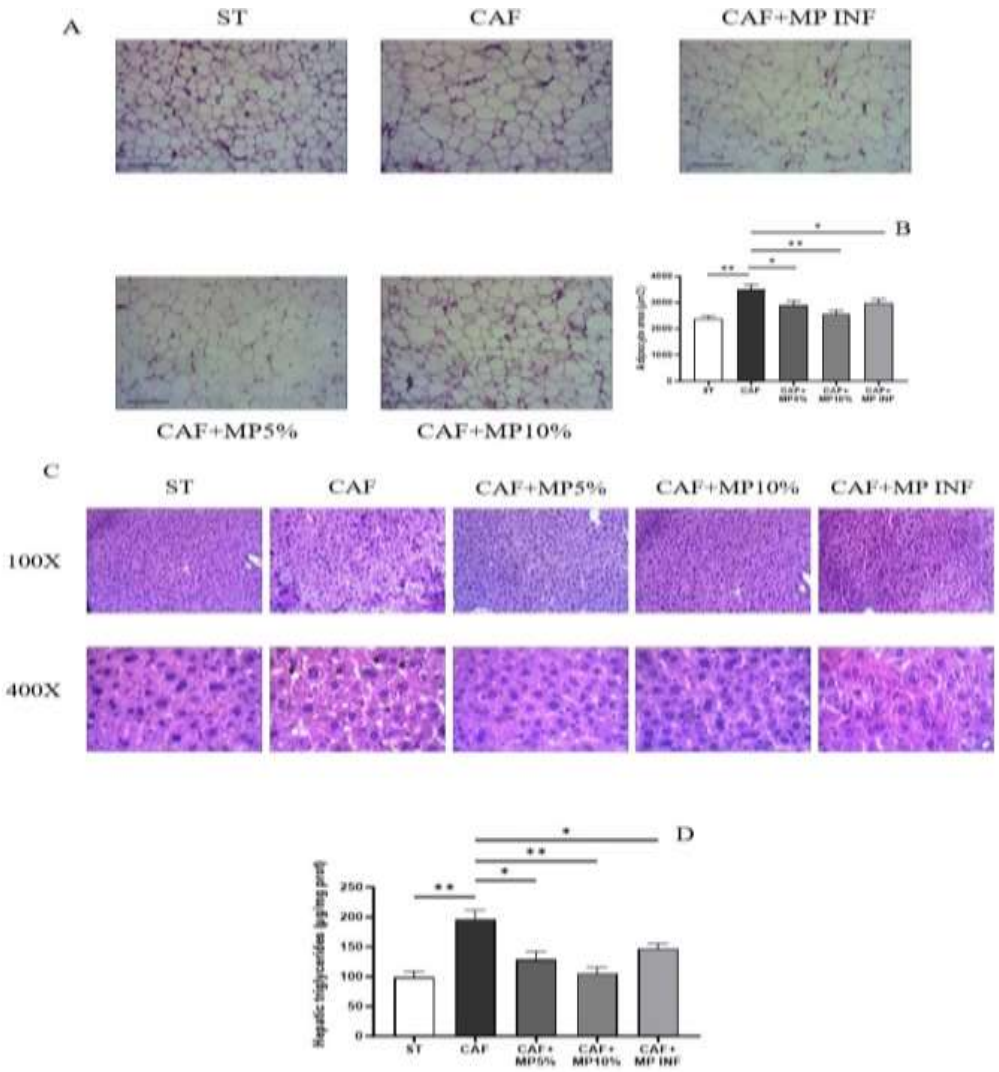

Figure 4: Effect of mandarin peel on epididymal adipose tissue and on the liver. (A) Representative histological images sections of epididymal adipose tissue stained H&E, captured in 100X (scale bar represents 200µm). (B) Adipocyte area determined by image J software. (C) Representative histological images sections of liver tissue stained H&E, captured in 100X and 400X. (D) Hepatic triglycerides measurements were performed using enzymatic colorimetric techniques, and were normalized to protein concentration. ST : Standard diet, CAF : Cafeteria diet, MP : Mandarin peel, MP INF : MP Infusion. Data are expressed as the mean ± SEM (n=8). * P ≤ 0.05; ** P ≤ 0.01 indicates significant differences compared with the only CAF group

Mandarin peel modifies the volume of epididymal adipose tissue and prevents the development of early hepatic steatosis

Obesity is often associated with an accumulation of visceral fat associated with adipocyte hypertrophy, and accumulation of fat in the liver, leading to non-alcoholic fatty liver disease (NAFLD).[39,40] To evaluate the effect of mandarin peel powder and infusion on adipose tissue size and on hepatic steatosis, histological analysis was used. The CAF diet promoted adipocyte hypertrophy with a significant increase of adipocyte area compared to the ST diet (Figures 4A and B). This effect was prevented by supplementation with 5% and 10% mandarin peel powder and mandarin peel infusion (Figures 4A and B). In the liver, the mice fed a CAF diet exhibited early hepatic steatosis, characterized by the appearance of pre-macrovacuolar lipid droplets compared to mice fed a ST diet (Figure 4C). However, supplementation with mandarin peel powder at 5% and 10% or mandarin peel infusion reduced the appearance of lipid droplets in the livers of mice (Figure 4C). The hepatic triglycerides (TG) levels were also measured. The CAF fed mice had significantly higher levels of hepatic TG ($P < 0.01$) compared to the ST fed mice (Figure 4D). However, in the group supplemented with mandarin peel powder at 5% and 10% or mandarin peel infusion, there were significantly decreased hepatic TG levels ($P < 0.05$ and $P < 0.01$) compared to the CAF group (Figure 4D). The results regarding the induction of the cafeteria diet in adipocyte hypertrophy and fatty liver disease have already been demonstrated by various studies.[30,41] However, studies such as Zunili ke et al. and Meiyi Hu et al. have demonstrated the beneficial effects of extract compounds obtained through chemical extraction (alcohol/ethyl acetate extraction method) of mandarin peel, as well as the effects of peel powder from other *citrus* fruits, on hepatic steatosis and adipocyte hypertrophy in animal models subjected to a high-fat diet.[38,42] Thus, Mandarin peel may also possess protective effects against lipogenesis and hepatic steatosis.

Our studies have shown that mandarin peel from the west Algerian cultivation prevents the obesogenic effect of a cafeteria diet in mice. The mandarin peel contains fiber, mainly pectin, essential oil rich in limonene and limonoid components, polyphenols, including flavonoids, vitamins, and carotenoids.[10,11,16] It would thus be essential in the prevention of obesity. The literature describes these compounds as potent antioxidants and anti-inflammatory agents, highlighting their effects on fat accumulation, improvement of lipid and glycemic profile parameters, and probably protection against obesity-associated hepatic steatosis.[9,14,15,20] Some flavonoids that are abundant in mandarin peel have been extensively studied, with hesperidin, narirutin, and nobiletin

demonstrating their effectiveness in reducing fat accumulation, combating obesity, and managing dyslipidemia and hyperglycemia.[20,21,43,44] Flavonoids and phenolic acid, which are abundant in *citrus* peels, can reduce fat absorption in the intestine while modulating the gut microbiota associated with obesity.[45] They also exert anti-obesity effects by modulating lipid metabolism parameters, inhibiting lipogenesis enzymes and stimulating lipolysis, while promoting the degradation of triglycerides stored in adipocytes.[46–48] In addition, these compounds inhibit adipogenesis, and promote the differentiation into brown adipocytes by acting on signaling and proliferation pathways.[46–48] Studies have shown that extracts from *citrus* peels, including mandarin, which are rich in polyphenols and essential oils, improve lipid metabolism hemostasis and enhance insulin sensitivity and hyperglycemia by regulating the expression and activation of genes related to lipogenesis, lipolysis, adipogenesis, and glycolysis.[36,49,50]

In addition to its anti-obesity potential, mandarin peel contains bioactive compounds that are potent antioxidants and anti-inflammatory agents. Thus, the mandarin peel may provide a broader therapeutic spectrum and serves as an asset in the diet, contributing to the improvement of metabolic and cardiovascular health.

Conclusion

Our investigation demonstrates the preventive effect of mandarin (*citrus reticulata*) peels in powdered form and as an infusion from the western region of Algeria on obesity. The mandarin peel prevents overweight conditions and also inhibits fat accumulation. Furthermore, this condiment helps regulate dyslipidemia and blood glucose levels, and reduces hepatic steatosis. Whether in different doses as powder or as an infusion, both methods appear to be effective in obesity prevention although the powder form may be more effective. However, consumption of more than two days per week in infusion form could have a better effect on lipid and glucose levels parameters. Thus, our study underscores the importance of using mandarin peel either as a food condiment or as a form of phytotherapy, because it could be an effective and natural strategy to promote metabolic and cardiovascular health due to the anti-inflammatory, antioxidant, and anti-obesity properties of its bioactive coumpounds. Looking ahead, mandarin peel could be the focus of more in-depth studies and advanced animal experimentation that may lead to clinical studies, highlighting its beneficial effects in obese individuals while adjusting the necessary doses.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgements

The authors gratefully acknowledge Dr. Kahia for his contribution and for the hospitality provided in his laboratory.

References

1. M Blüher. Obesity: global epidemiology and pathogenesis. Nat. Rev. Endocrinol. 2019; 15(5):288–298. doi:10.1038/s41574-019-0176-8.
2. X Lin, H Li. Obesity: Epidemiology, Pathophysiology, and Therapeutics. Front. Endocrinol. 2021; 12:706978. doi:10.3389/fendo.2021.706978.
3. C Koliaki, S Liatis, A Kokkinos. Obesity and cardiovascular disease: revisiting an old relationship. Metabolism. 2019; 92:98–107. doi:10.1016/j.metabol.2018.10.011.
4. G Battineni, GG Sagaro, N Chintalapudi, F Amenta, D Tomassoni, SK Tayebati. Impact of Obesity-Induced Inflammation on Cardiovascular Diseases (CVD). Int. J. Mol. Sci. 2021; 22(9):4798. doi:10.3390/ijms22094798.
5. M Prats-Arimon, M Puig-Llobet, O Barceló-Peiró, I Ribot-Domènech, C Vilalta-Sererols, B Fontecha-Valero, M Heras-Ojeda, Z Agüera, T Lluch-Canut, A Moreno-Poyato, MC Moreno-Arroyo. An Interdisciplinary Intervention Based on Prescription of Physical Activity, Diet, and Positive Mental Health to Promote Healthy Lifestyle in Patients with Obesity: A Randomized Control Trial. Nutrients. 2024; 16(16):2776. doi:10.3390/nu16162776.
6. AM Chao, KM Quigley, TA Wadden. Dietary interventions for obesity: clinical and mechanistic findings. J. Clin. Invest. 2021; 131(1):e140065, 140065. doi:10.1172/JCI140065.
7. A Purwanto, A Adji, A Yanuarita, B de Liyis, B Suwito, S Haksama. An Evidence-Based Review of Herbal Medications in Cardiovascular Disease: A Systematic Review. Trop. J. Nat. Prod. Res. 2025; 9(7):3404–3412. doi:10.26538/tjnpr/v9i7.69.
8. E Santali, N Ichoron, JV Anyam, JO Igoli. Spectroscopic Evaluation of Unsaturation in Some Medicinal Plant Seed Oils: doi.org/10.26538/tjnpr/v6i8.11. Trop. J. Nat. Prod. Res. 2022; 6(8):1223–1227.
9. P Deng, J Durham, J Liu, X Zhang, C Wang, D Li, T Gwag, M Ma, B Hennig. Metabolomic, Lipidomic, Transcriptomic, and Metagenomic Analyses in Mice Exposed to PFOS and Fed Soluble and Insoluble Dietary Fibers. Environ. Health Perspect. 2022; 130(11):117003. doi:10.1289/EHP11360.
10. N Durmus, Z Gulsunoglu-Konuskan, M Kilic-Akyilmaz. Recovery, Bioactivity, and Utilization of Bioactive Phenolic Compounds in *Citrus* Peel. Food Sci. Nutr. 2024; 12(12):9974–9997. doi:10.1002/fsn3.4570.
11. FB Oluwatobi, OB Afolabi, PA Okiki, OB Akpor. Biological Properties And GC-MS Identification of Compounds of Ethanol Extracts and Volatile Oils From *Citrus sinensis*, *Citrus paradisi* and *Citrus reticulata*. Trop. J. Nat. Prod. Res. 2024; 8(9):8453–8460. doi:10.26538/tjnpr/v8i9.30.
12. A Idoko, EJ Parker, OU Njoku. Assessment of the Effect of Flavonoids Biomolecules on Fat Mass and Obesity Associated (FTO) Protein as Anti-Obesity Agents: An In-Silico Study. Trop. J. Nat. Prod. Res. 2024; 8(3):6669–6680. doi:10.26538/tjnpr/v8i3.29.
13. A Ullah, Q Sun, J Li, J Li, P Khatun, G Kou, Q Lyu. Bioactive Compounds in *Citrus reticulata* Peel Are Potential Candidates for Alleviating Physical Fatigue through a Triad Approach of Network Pharmacology, Molecular Docking, and Molecular Dynamics Modeling. Nutrients. 2024; 16(12):1934. doi:10.3390/nu16121934.
14. M Alcalá, I Sánchez-Vera, J Sevillano, L Herrero, D Serra, MP Ramos, M Viana. Vitamin E reduces adipose tissue fibrosis, inflammation, and oxidative stress and improves metabolic profile in obesity. Obes. Silver Spring Md. 2015; 23(8):1598–1606. doi:10.1002/oby.21135.
15. Y Yao, HM Goh, JE Kim. The Roles of Carotenoid Consumption and Bioavailability in Cardiovascular Health. Antioxidants. 2021; 10(12):1978. doi:10.3390/antiox10121978.
16. L Kamaliroosta, M Zolfaghari, S Shafiee, K Larijani, M Zojaji. Chemical Identifications of *Citrus* Peels Essential Oils. 2016; 6:69–76.
17. MA Castro, MA Llanos, BE Rodenak-Kladniew, L Gavernet, ME Galle, R Crespo. *Citrus reticulata* peel oil as an antiatherogenic agent: Hypolipogenic effect in hepatic cells, lipid storage decrease in foam cells, and prevention of LDL oxidation. Nutr. Metab. Cardiovasc. Dis. Nutr Metab Cardiovasc Dis.. 2020; 30(9):1590–1599. doi:10.1016/j.numecd.2020.04.033.
18. M Shi, Q Guo, Z Xiao, null Sarengaowa, Y Xiao, K Feng. Recent Advances in the Health Benefits and Application of Tangerine Peel (*Citri Reticulatae Pericarpium*): A Review. Foods Basel Switz. 2024; 13(13):1978. doi:10.3390/foods13131978.
19. OM Ahmed, MA Hassan, SM Abdel-Twab, MN Abdel Azeem. Navel orange peel hydroethanolic extract, naringin and naringenin have anti-diabetic potentials in type 2 diabetic rats.

Biomed. Pharmacother. Biomedecine Pharmacother. 2017; 94:197–205. doi:10.1016/j.biopha.2017.07.094.
20. H Xiong, J Wang, Q Ran, G Lou, C Peng, Q Gan, J Hu, J Sun, R Yao, Q Huang. Hesperidin: A Therapeutic Agent For Obesity. Drug Des. Devel. Ther. 2019; 13:3855–3866. doi:10.2147/DDDT.S227499.
21. ST Im, H Kang, J Kim, S-R Kim, K-N Kim, S-H Lee. Narirutin-Rich Celluclast Extract from Mandarin (*Citrus unshiu*) Peel Alleviates High-Fat Diet-Induced Obesity and Promotes Energy Metabolism in C57BL/6 Mice. Int. J. Mol. Sci. 2024; 25(8):4475. doi:10.3390/ijms25084475.
22. N Sukkasem, W Chatuphonprasert, K Jarukamjorn. Hesperidin and Myricetin Attenuated Non-Alcoholic Fatty Liver Disease (NAFLD) in HepG2 Cells: doi.org/10.26538/tjnpr/v4i10.14. Trop. J. Nat. Prod. Res. 2020; 4(10):739–747.
23. S-J Leigh, MD Kendig, MJ Morris. Palatable Western-style Cafeteria Diet as a Reliable Method for Modeling Diet-induced Obesity in Rodents. J. Vis. Exp. JoVE. 2019; (153). doi:10.3791/60262.
24. C Darimont, M Turini, M Epitaux, I Zbinden, M Richelle, E Montell, A Ferrer-Martinez, K Macé. beta3-adrenoceptor agonist prevents alterations of muscle diacylglycerol and adipose tissue phospholipids induced by a cafeteria diet. Nutr. Metab. 2004; 1(1):4. doi:10.1186/1743-7075-1-4.
25. L-H Li, EP Dutkiewicz, Y-C Huang, H-B Zhou, C-C Hsu. Analytical methods for cholesterol quantification. J. Food Drug Anal. 27(2):375–386. doi:10.1016/j.jfda.2018.09.001.
26. N Fukuyama, K Homma, N Wakana, K Kudo, A Suyama, H Ohazama, C Tsuji, K Ishiwata, Y Eguchi, H Nakazawa, E Tanaka. Validation of the Friedewald Equation for Evaluation of Plasma LDL-Cholesterol. J. Clin. Biochem. Nutr. 2008; 43(1):1–5. doi:10.3164/jcbn.2008036.
27. VG Yuen, JH McNeill. Comparison of the glucose oxidase method for glucose determination by manual assay and automated analyzer. J. Pharmacol. Toxicol. Methods. 2000; 44(3):543–546. doi:10.1016/s1056-8719(01)00117-4.
28. A Picca, V Pesce, F Fracasso, A-M Joseph, C Leeuwenburgh, AMS Lezza. A comparison among the tissue-specific effects of aging and calorie restriction on TFAM amount and TFAM-binding activity to mtDNA in rat. Biochim. Biophys. Acta. 2014; 1840(7):2184–2191. doi:10.1016/j.bbagen.2014.03.004.
29. JE Noble, MJA Bailey. Quantitation of protein. Methods Enzymol. 2009; 463:73–95. doi:10.1016/S0076-6879(09)63008-1.
30. Y Buyukdere, A Gulec, A Akyol. Cafeteria diet increased adiposity in comparison to high fat diet in young male rats. PeerJ. 2019; 7:e6656. doi:10.7717/peerj.6656.
31. Y Qian, Z Gao, C Wang, J Ma, G Li, F Fu, J Guo, Y Shan. Effects of Different Treatment Methods of Dried *Citrus* Peel (Chenpi) on Intestinal Microflora and Short-Chain Fatty Acids in Healthy Mice. Front. Nutr. 2021; 8:702559. doi:10.3389/fnut.2021.702559.
32. Y-C Chou, C-T Ho, M Pan. Immature *Citrus reticulata* Extract Promotes Browning of Beige Adipocytes in High-Fat Diet-Induced C57BL/6 Mice. J. Agric. Food Chem. 2018; 66 37:9697–9703. doi:10.1021/acs.jafc.8b02719.
33. J Vekić, A Zeljković, A Stefanović, Z Jelić-Ivanović, V Spasojević-Kalimanovska. Obesity and dyslipidemia. Metabolism. 2019; 92:71–81. doi:10.1016/j.metabol.2018.11.005.
34. Q Chen, A Abudukeremu, K Li, M Zheng, H Li, T Huang, C Huang, K Wen, Y Wang, Y Zhang. High-Density Lipoprotein Subclasses and Their Role in the Prevention and Treatment of Cardiovascular Disease: A Narrative Review. Int. J. Mol. Sci. 2024; 25(14):7856. doi:10.3390/ijms25147856.
35. L Wang, H Xu, F Yuan, Q Pan, R Fan, Y Gao. Physicochemical characterization of five types of *citrus* dietary fibers. Biocatal. Agric. Biotechnol. 2015; 4:250–258. doi:10.1016/J.BCAB.2015.02.003.
36. J Guo, H Tao, Y Cao, C-T Ho, S Jin, Q Huang. Prevention of Obesity and Type 2 Diabetes with Aged *Citrus* Peel (Chenpi) Extract. J. Agric. Food Chem. 2016; 64 10:2053–2061. doi:10.1021/acs.jafc.5b06157.
37. Y Tung, W-T Chang, S Li, J-C Wu, V Badmeav, C-T Ho, M Pan. *Citrus* peel extracts attenuated obesity and modulated gut microbiota in mice with high-fat diet-induced obesity. Food Funct. 2018; 9 6:3363–3373. doi:10.1039/c7fo02066j.
38. Z Ke, Y Zhao, S Tan, H Chen, Y Li, Z Zhou, C Huang. *Citrus reticulata* Blanco peel extract ameliorates hepatic steatosis, oxidative stress and inflammation in HF and MCD diet-induced NASH C57BL/6 J mice. J. Nutr. Biochem. 2020; 83:108426. doi:10.1016/j.jnutbio.2020.108426.
39. S Polyzos, J Kountouras, C Mantzoros. Obesity and nonalcoholic fatty liver disease: From pathophysiology to therapeutics. Metabolism. 2019; 92:82–97. doi:10.1016/j.metabol.2018.11.014.
40. U White. Adipose tissue expansion in obesity, health, and disease. Front. Cell Dev. Biol. 2023; 11:1188844. doi:10.3389/fcell.2023.1188844.
41. FRS Gasparin, FO Carreño, JM Mewes, EH Gilglioni, CLS Pagadigorria, MRM Natali, KS Utsunomiya, RP Constantin, AT Ouchida, C Curti, IC Gaemers, RPJO Elferink, J Constantin, EL Ishii-Iwamoto. Sex differences in the development of hepatic steatosis in cafeteria diet-induced obesity in young mice. Biochim. Biophys. Acta Mol. Basis Dis. 2018; 1864(7):2495–2509. doi:10.1016/j.bbadis.2018.04.004.
42. M Hu, L Zhang, Z Ruan, P Han, Y Yu. The Regulatory Effects of *Citrus* Peel Powder on Liver Metabolites and Gut Flora in Mice with Non-Alcoholic Fatty Liver Disease (NAFLD). Foods Basel Switz. 2021; 10(12):3022. doi:10.3390/foods10123022.
43. X Li, R Zhuang, Z Lu, F Wu, X Wu, K Zhang, M Wang, W Li, H Zhang, W Zhu, B Zhang. Nobiletin promotes lipolysis of white adipose tissue in a circadian clock-dependent manner. J. Nutr. Biochem. 2024; 132:109696. doi:10.1016/j.jnutbio.2024.109696.
44. TTA Bui, MTT Do, STT Do, TT Nguyen, CD Duong. Simultaneous Analysis Method for Rutin, Diosmin, Hesperidin, and Quercetin in Solid Food Supplements by HPLC-PDA. Trop. J. Nat. Prod. Res. 2025; 9(2):473–479. doi:10.26538/tjnpr/v9i2.9.
45. M Falduto, F Smedile, M Zhang, T Zheng, J Zhu, Q Huang, R Weeks, AM Ermakov, ML Chikindas. Anti-obesity effects of Chenpi: an artificial gastrointestinal system study. Microb. Biotechnol. 2022; 15(3):874–885. doi:10.1111/1751-7915.14005.
46. X Zhang, X Li, H Fang, F Guo, F Li, A Chen, S Huang. Flavonoids as inducers of white adipose tissue browning and thermogenesis: signalling pathways and molecular triggers. Nutr. Metab. 2019; 16:47. doi:10.1186/s12986-019-0370-7.
47. A Rufino, VM Costa, F Carvalho, E Fernandes. Flavonoids as antiobesity agents: A review. Med. Res. Rev. 2020; 41:556–585. doi:10.1002/med.21740.
48. K Lu, YM Yip. Therapeutic Potential of Bioactive Flavonoids from *Citrus* Fruit Peels toward Obesity and Diabetes Mellitus. Future Pharmacol. 2023; 3(1):14–37. doi:10.3390/futurepharmacol3010002.
49. K Feng, X Zhu, G Liu, Q Kan, T Chen, Y Chen, Y Cao. Dietary *citrus* peel essential oil ameliorates hypercholesterolemia and hepatic steatosis by modulating lipid and cholesterol homeostasis. Food Funct. 2020; 11(8):7217–7230. doi:10.1039/d0fo00810a.
50. J Zou, Q Song, PC Shaw, Y Wu, Z Zuo, R Yu. Tangerine Peel-Derived Exosome-Like Nanovesicles Alleviate Hepatic Steatosis Induced by Type 2 Diabetes: Evidenced by Regulating Lipid Metabolism and Intestinal Microflora. Int. J. Nanomedicine. 2024; 19:10023–10043. doi:10.2147/IJN.S478589.