Int. J. Plant Bas. Pharm. (2023) 3(1), 54-61

INTERNATIONAL JOURNAL OF PLANT BASED PHARMACEUTICALS

https://ijpbp.com

RESEARCH ARTICLE

OPEN ACCESS

The inclusion of garlic and turmeric powder in high-fructose diets protects against the development of metabolic syndrome in Wistar rats

Ali Siddiq Idoko[a*], Aliyu Abdullahi[b], Masud Eneji Sadiq[c], Bilkis Muhammad Maibalangu[d]

[a] *Federal University Dutsin-Ma, Department of Biochemistry and Molecular Biology, Katsina State, Nigeria*
[b] *Alqalam University, Department of Biological Sciences, Katsina State, Nigeria*
[c] *Usmanu Danfodiyo University, Department of Biochemistry and Molecular Biology, Sokoto, Nigeria*
[d] *College of Education Azare, Department of Chemistry, Bauchi State, Nigeria*

ARTICLE INFO

Article History:

Received: 10 September 2022
Revised: 26 October 2022
Accepted: 25 November 2022
Available online: 02 December 2022

Edited by: B. Tepe

Keywords:

Metabolic syndrome
Turmeric
Garlic
Dyslipidaemia
Insulin resistance
Oxidative stress

ABSTRACT

The worldwide prevalence of the metabolic syndrome is largely attributable to excessive consumption of high-energy food sweeteners and lifestyle practices that encourage physical inactivity. This study was designed to evaluate the potential benefits of garlic and/or turmeric in down-regulating the risk factors associated with metabolic syndrome. Twenty-four male Wistar rats were divided into 8 groups of 3 rats per group. Group 1 received standard rat chow, Group 2 received a high-fructose diet only, while Group 3 received a 2% turmeric-supplemented high-fructose diet. Groups 4 and 5 were fed a standard diet supplemented with 2% each of garlic and turmeric:garlic (50% w/w), respectively. Groups 6, 7, and 8 were respectively fed a high-fructose diet supplemented with 2% garlic, a standard diet supplemented with 2% turmeric, and a high-fructose diet supplemented with 2% turmeric:garlic (50% w/w). Feed intake and changes in body weight were monitored weekly and after 56 days, the rats were sacrificed. Activities of serum antioxidant enzymes, lipid profile, and atherogenic indices were determined. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was computed from the measured blood glucose and insulin levels. The positive control (Group 2) gained weight significantly ($p < 0.05$) when compared with groups that received diet supplementation. Total cholesterol, triglycerides, low-density lipoprotein, and atherogenic indices of diet-supplemented groups were significantly low ($p < 0.05$) when compared with the positive control. Interestingly, while no differences ($p > 0.05$) were observed in the catalase and glutathione peroxidase enzyme activities in the high-fat diet group supplemented with 2% mixed turmeric:garlic when compared with the normal control, activities of these enzymes in the garlic and/or turmeric supplemented high-fructose diet groups were significantly elevated ($p < 0.05$) when compared with the positive control. The HOMA-IR and atherogenic indices results revealed the inclusion of turmeric and garlic in a high-fat diet had anti-dyslipidemic effects, decreased oxidative stress, and reduced coronary risk factors. Our findings strongly suggest supplementation of high-calorie diets with garlic and/or turmeric powder has potential long-term health benefits in individuals exposed to the risks of developing metabolic syndrome.

Reviewed by:
Khalid Hussain: University of Punjab, Lahore, Pakistan
Manobendro Nath Ray: University of Rajshahi, Rajshahi, Bangladesh
Teeraporn Katisart: Mahasarakham University, Maha Sarakham, Thailand
* Corresponding author(s):
E-mail address:
asidoko1@gmail.com (A. S. Idoko)
e-ISSN: 2791-7509
doi: https://doi.org/10.29228/ijpbp.16

1. Introduction

Unhealthy lifestyles such as smoking, alcoholism, and overconsumption of sweetened beverages are increasing the prevalence of metabolic syndrome (MetS); a cluster of risk factors for the development of cardiovascular-related diseases. The clustering abnormalities often include hyperglycemia, dyslipidemia, central obesity, insulin resistance, and high blood pressure (Alberti et al., 2009) which individually or synergistically increase the risk of cardiovascular complications (Sperling et al., 2015; Tune et al., 2017).

Please cite this article as: Idoko, A. S., Abdullahi, A., Sadiq, M. E., & Maibalangu, B. M. (2023). The inclusion of garlic and turmeric powder in high-fructose diets protects against the development of metabolic syndrome in Wistar rats. *International Journal of Plant Based Pharmaceuticals*, *3*(1), 54-61, https://doi.org/10.29228/ijpbp.16.

Although the global prevalence of the syndrome is about 25% and 19% in the populations of adults and children respectively (do Vale Moreira et al., 2020), it is feared that the prevalence could hit 53% by the year 2035 (Gierach et al., 2014). Despite the varied definitions of MetS, the disease prevalence notwithstanding correlates positively with increasing body mass index (Engin, 2017; Nguyen et al., 2008). Central obesity (visceral adiposity) usually caused by overfeeding and excessive consumption of sweetened beverages triggers inflammation and oxidative stress (Huang et al., 2015; Rehman & Akash, 2016). These two conditions can individually and collectively cause cardiovascular damage directly or activate pathways that result in the development of the syndrome (Pekgor et al., 2019).

Since unhealthy lifestyle such as overfeeding and consumption of alcohol and sweetened drinks predisposes to metabolic syndrome, lifestyle modifications including the consumption of antioxidant-rich functional foods could be helpful in the management of MetS (Rodriguez-Cano et al., 2015; Tian et al., 2018). Existing literature on garlic and turmeric suggests these spices possess remarkable antioxidant properties (Anand et al., 2007; Coban et al., 2012; Panyod & Sheen, 2020). The present study, therefore, explores the potential benefits of garlic and turmeric both singly and in combination as food supplements in mitigating the effects of high-fat diet predisposition to MetS.

2. Materials and methods

2.1. Chemicals and feed ingredients

All the chemicals and reagents including methionine, premix minerals, and vitamins used were of analytical grades. Commercial assay kits for antioxidant enzymes (Cayman Chemical Michigan, USA), lipid profile, and insulin ELISA kits (Randox Laboratories Ltd., UK) were purchased for biochemical assays. Feed ingredients including rice bran, corn starch, bone meal, soybean meal, and palmitic acid (16:0) were sourced locally from Dutsin-Ma Central Market, Katsina State.

Table 1. Composition of formulated rat diet

Feed ingredient	Control diet g/100 g	High-fructose g/100 g
Corn starch	55.45	-
Fructose	-	55.45
Soybean meal	32	32
Cellulose	4.50	4.50
Palm oil	6	6
Bone meal	1.25	1.25
Salt mix	0.30	0.30
Vitamin/mineral mix	0.25	0.25
Methionine	0.25	0.25
Total	100	100

Mineral mix (g/kg): $CaCO_3$ (15.258), $COCl_2.6H_2O$ (0.001), $ZnCl_2$ (0.001), $CuSO_4.5H_2O$ (0.019), $FeSO_4.7H_2O$ (1.078), $MgSO_4$ (2.929), $MnSO_4.2H_2O$ (0.178), KI (0.032), KH_2PO_4 (15.559), and NaCl (5.573), Vitamin mix (g/kg diets): thiamine (0.02), riboflavin (0.03), pyridoxine (0.01), *p*-aminobenzoic acid (0.20), myo-inositol (2.00), biotin (0.001), menadione (0.01), ergocalciferol (0.4), choline-HCl (2.0), and cellulose (3.31), α–tocopherol acetate (50), retinal palmitate (0.4), calcium pantothenate (0.0016), and folic acid (0.0002)

2.2. Spice supplements

Turmeric and garlic were bought from Dutsin-Ma Central Market in the Katsina State of Nigeria and were identified as *Curcuma longa* (FUDMA/PSB/00143) and *Allium sativum* (FUDMA/PSB/0019) in the Herbarium of the Department of Biological Sciences, Federal University Dutsin-Ma (FUDMA) The spices were carefully screened, washed, air dried then pulverized using electronic blender and finally sieved through a 0.05 mm sieve. Equal amounts (w/w) of the processed spices were mixed and stored in air-tight containers.

2.3. Formulation of the standard rat diet

Standard rat chow was formulated following the methods of Idoko et al. (2022) and Imam et al. (2022). Briefly, corn starch, cellulose, soybean meal (SBM), vitamin, and mineral mix, were mixed as summarized in Table 1.

2.4. Supplementation of formulated diet

The formulated standard diet was mixed with garlic, turmeric, and garlic:turmeric powders in the ratio 98:2 (w/w) to obtain a 2% spice-supplemented diet.

2.5. Experimental design

Male Wistar rats (24) with an average weight of 120 ± 5.20 g were purchased from National Veterinary Research Institute, Vom, Plateau State, Nigeria. The animals were housed in plastic cages and were maintained according to the guidelines of the National Research Council (2011) for experimental animals. As previously described (Idoko et al., 2022), the rats were divided into 8 groups of 3 rats per group and the formulated diets were randomly assigned as follows:

Group 1 = Standard diet (normal control)
Group 2 = High-fructose diet (positive control)
Group 3 = High-fructose diet + 2% turmeric
Group 4 = Standard diet + 2% garlic
Group 5 = Standard diet + 2% mixed turmeric:garlic (50% w/w)
Group 6 = High-fructose diet + 2% garlic
Group 7 = Standard diet + 2% turmeric
Group 8 = High-fructose diet + 2% mixed turmeric:garlic (50% w/w)

Feeding was ad libitum for a period of eight (8) weeks.

2.6. Determination of feed intake and change in body weight

The rats were fed three times daily and feed was withdrawn two hours after access. The weekly feed intake was estimated by subtracting the leftover amount from the total amount served. The rats were also weighed weekly to estimate the change in body weights.

2.7. Blood sample collection

On the 56th day of the experiment, the rats were weighed, anesthetized, and sacrificed by cutting the jugular vein after a 12-

hour fasting period. Blood was collected in plain sample containers and then centrifuged at 1500 g for 15 minutes to obtain serum for further biochemical analyses.

2.8. Determination of insulin and HOMA-IR

The blood glucose levels were determined using a glucometer (Acuu chek) according to the manufacturer`s protocol. ELISA kit was used to determine serum insulin levels while the index for Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated as follows (Yin et al., 2013):

$$HOMA-IR = \frac{fasting\ insulin\ (mU/l) x\ fasting\ glucose\ (mmol/l)}{22.5} x\ Concentration\ of\ standard$$

2.9. Determination of lipid profile parameters

2.9.1. Determination of total cholesterol (TC)

Serum total cholesterol was estimated spectrophotometrically using Randox kits following methods described by the manufacturer. Briefly, 10 µl of serum was added to 1000 µl of the reagent (4-aminoantipyrine, phenol, peroxidase, cholesterol esterase, cholesterol oxidase, and PIPES buffer) in a tube. A standard was similarly prepared by adding 10 µl of the standard reagent to 1000 µl of the reagent. Finally, the blank solution for instrument calibration was equally constituted by replacing serum with 10 µl distilled water. Prepared solutions were incubated at 37 °C for 5 minutes after which absorbance was taken at 546 nm. Total cholesterol (mg/dl) was calculated using the relationship:

$$Total\ Cholesterol\ \left(\frac{mg}{dl}\right) = \frac{Absorbance\ of\ sample}{Absorbance\ of\ standard} x\ Concentration\ of\ standard$$

2.9.2. Determination of serum triglycerides (TG)

Serum triglyceride concentration was determined based on an enzymatic hydrolysis procedure using Randox kits as described by the manufacturer. To 10 µl of a serum sample, 1000 µl of reagent (4-amonophenazone, ATP, lipases, glycerol-kinase, glycerol-3-phosphate oxidase, and peroxidase, PIPES buffer, 4-chloro-phenol, and magnesium-ions) was added. Similar preparations were done for the standard solution (1000 µl of the reagent + 10 µl of the standard reagent) and blank (1000 µl + 10 µl distilled water). These were mixed properly and the absorbance of the sample was read against the blank at 546 nm. Triglyceride concentration was calculated as follows:

$$Triglyceride\ concentration\ \left(\frac{mg}{dl}\right) = \frac{Absorbance\ of\ sample}{Absorbance\ of\ standard} x\ Concentration\ of\ standard$$

2.9.3. Determination of HDL-cholesterol (HDL-C)

High-density lipoprotein-cholesterol (HDL-cholesterol) was determined based on first-stage quantitative precipitation of low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and chylomicron fractions by the addition of phosphotungstic acid in the presence of magnesium ions. The second stage involves the CHOP-PAP assay as described by the manufacturer. Two separate tubes containing 200 µl each of serum sample and standard were mixed with 500 µl of Randox kit reagent (phosphotungstic acid and magnesium chloride), incubated at 28 °C for 10 minutes then centrifuged at 4000 rpm for 10 minutes. For the second stage estimation of HDL-cholesterol, exactly 100 µl of recovered supernatants were mixed with 1000 µl of working reagent. A blank solution was similarly prepared using 10 µl of distilled water. The reaction constituents in each tube were thoroughly mixed and incubated at 37 °C for 5 minutes. The absorbance was read at 546 nm and HDL-cholesterol was estimated using the relationship:

$$HDL-C\ \left(\frac{mg}{dl}\right) = \frac{Absorbance\ of\ sample}{Absorbance\ of\ standard} x\ Concentration\ of\ standard$$

2.9.4. Determination of LDL-Cholesterol (LDL-C)

Low-density lipoprotein-cholesterol (LDL-cholesterol) was calculated from estimated values obtained from TC, TG, and HDL assays (Friedewald et al., 1972):

$$LDL-C\ \left(\frac{mg}{dl}\right) = \text{TC} - \frac{TG}{5} - HDL-C$$

The method of Kazemi et al. (2018) was used to calculate the atherogenic index (AI) and coronary risk index (CRI) as follows:

$$Atherogenic\ Index\ (AI) = \frac{LDL-C}{HDL-C}$$

$$Coronary\ risk\ index\ (CRI) = \frac{TC}{HDL-C}$$

2.10. Determination of the serum antioxidant enzymes

2.10.1. Superoxide dismutase (SOD) assay

The determination was based on using tetrazolium salt to detect superoxide radicals produced by the action of xanthine oxidase on hypoxanthine. Exactly 200 µl of the appropriately diluted radical detector was pipetted into well-labeled microtitre plate wells after which 10 µl each of the prepared standard and serum samples were added in separate wells. The reaction in each well was initiated by dispensing 20 µl diluted xanthine oxidase. The wells were then covered and incubated on a shaker at room temperature for 20 minutes. The absorbance was read at 450 nm using Rayto (RT 6000) plate reader.

2.10.2. Determination of serum catalase activity

The 4-amino-3-hydrazino-5-mercapto-1,2,4-triazole (Purpald) spectrophotometric method was used to determine catalase activity. Into three microtiter wells labeled sample, standard, and control, 100 µl of assay buffer and 30 µl of methanol were added. Twenty microliters of each of the prepared standard and serum samples were added into appropriate wells, then 20 µl H_2O_2 was added to each well to initiate the reaction. The plate was covered and incubated on a shaker for 20 minutes at room temperature after which KOH (30 µl) was added to each well to terminate the reaction. This was followed by the addition of 30 µl of purpald chromogen. The plate was incubated on a shaker for 10 minutes at room temperature. Potassium periodate (10 µl) was pipetted into each well and incubated on a shaker for another 5 minutes and the absorbance was read at 540 nm using Rayto (RT 6000) plate reader.

2.10.3. Determination of glutathione peroxidase activity

Glutathione peroxidase activity was determined by a coupling reaction with glutathione reductase. Oxidized glutathione is produced when hydroperoxide is reduced by glutathione peroxidase. The oxidized glutathione is recycled to its reduced form by the action of glutathione reductase in the presence of NADPH. This decreases the absorbance at 340 nm. Briefly, a microtitre plate was prepared by adding 20 µl serum sample, 100 µl of assay buffer, and 50 µl of the co-substrate mixture. A non-enzymatic well was similarly prepared to contain 50 µl of the co-substrate mixture and

120 µl of assay buffer. The positive control well contained 100 µl of assay buffer, 20 µl of diluted GPx, and 50 µl of the co-substrate mixture. The reaction was initiated by dispensing 20 µl of cumenehydroperoxide to each well. The plates were shaken for a few seconds. The decrease in absorbance was read at 340 nm using Rayto (RT-2100C) plate reader once every 3 minutes.

2.11. Statistical analysis

The results are presented as means ± standard error of the mean (SEM) for triplicate determinations. SPSS statistical software package for windows version 16 (IBM Corp.) was used for one-way analysis of variance (ANOVA) while means were compared for significance using posthoc Ducan's new multiple range test at 95% confidence interval.

3. Results and discussion

3.1. Feed intake, change in body weight, and HOMA-IR of experimental rats fed garlic and turmeric-supplemented diet

Table 2 presents the results of feed intake and body weight changes of experimental rats fed the high-fructose diet supplemented with garlic and turmeric. The positive control group (G2) consumed significantly more feed when compared with all other groups ($p < 0.05$) with a commensurate increased gain in body weight ($p < 0.05$). Feed consumed by groups fed high-fructose diets supplemented with 2% turmeric (G3), 2% mixed turmeric:garlic (G5), and standard diet + 2% mixed turmeric:garlic compared favorably ($p > 0.05$) with the standard diet normal control group (G1) while feed consumed by G4 (standard diet + 2% garlic), G6 (high-fructose diet + 2% garlic) and G7 (standard diet + 2% turmeric) in the range 328.54 ± 2.05 - 330.00 ± 1.10 g was significantly higher ($p < 0.05$) when compared to feed consumed by G1 (normal control). However, no differences in body weight changes ($p > 0.05$) were observed between groups G1, G4, G5, and G7 while the group with the least gain in body weights include G3 and G6 both of which received a high-fructose diet supplemented with 2% turmeric and 2% garlic respectively.

The values of blood glucose, insulin, and HOMA-IR were significantly ($p < 0.05$) lower in the groups fed supplemented diets when compared with the positive group (G2) as shown in Table 3. No differences were observed in the HOMA-IR values for groups that received standard diets with or without supplementation. Interestingly, circulating insulin and HOMA-IR values were observed for a high-fructose diet + 2% mixed turmeric:garlic (G8) compared ($p > 0.05$) with that observed for normal control (G1).

Table 2. Weight gain and feed intake by rats fed garlic and/or turmeric supplemented high-fructose diets

Group	Weight (g)	Feed intake (g)
G1	8.97 ± 1.70^{b}	324.66 ± 2.18^{a}
G2	17.86 ± 2.12^{c}	500.96 ± 2.17^{c}
G3	3.72 ± 1.13^{a}	321.58 ± 1.66^{a}
G4	10.44 ± 0.84^{b}	328.54 ± 2.05^{b}
G5	10.16 ± 3.09^{b}	313.36 ± 3.01^{a}
G6	2.68 ± 1.36^{a}	334.70 ± 1.32^{b}
G7	10.57 ± 2.89^{b}	330.00 ± 1.10^{b}
G8	8.55 ± 2.27^{b}	324.66 ± 3.01^{a}

Values are presented as mean ± SEM for 8 determinations. Values with different superscripts along the same column are significantly different ($p < 0.05$). Group 1 = Standard diet (normal control), Group 2 = High-fructose diet (positive control), Group 3 = High-fructose diet + 2% turmeric, Group 4 = Standard diet + 2% garlic, Group 5 = Standard diet + 2% mixed turmeric:garlic (50% w/w), Group 6 = High-fructose diet + 2% garlic, Group 7 = Standard diet + 2% turmeric; Group 8 = High-fructose diet +2% mixed turmeric:garlic (50% w/w)

Table 3. Glucose, insulin and homeostasis model assessment (HOMA-IR)

Group	Glucose (mmol/l)	Insulin (µU/l)	HOMA-IR
G1	4.59 ± 0.40^{d}	9.33 ± 0.33^{ab}	1.92 ± 0.24^{a}
G2	6.19 ± 0.67^{e}	26.67 ± 0.33^{e}	7.33 ± 0.07^{d}
G3	3.85 ± 0.81^{c}	15.33 ± 0.33^{c}	2.62 ± 0.76^{b}
G4	4.00 ± 0.24^{c}	9.67 ± 0.33^{ab}	1.71 ± 0.54^{a}
G5	4.31 ± 0.49^{c}	17.33 ± 0.33^{d}	3.32 ± 0.80^{c}
G6	3.94 ± 0.64^{c}	17.00 ± 0.58^{d}	2.98 ± 0.13^{c}
G7	4.46 ± 0.11^{d}	10.33 ± 0.33^{b}	2.05 ± 0.80^{a}
G8	4.93 ± 0.13^{d}	8.67 ± 0.33^{a}	1.90 ± 0.08^{a}

Values are presented as mean ± SEM for 3 determinations. Values with different superscripts along the same column are significantly different ($p < 0.05$). Group 1 = Standard diet (normal control), Group 2 = High-fructose diet (positive control), Group 3 = High-fructose diet + 2% turmeric, Group 4 = Standard diet + 2% garlic, Group 5 = Standard diet + 2% mixed turmeric:garlic (50% w/w), Group 6 = High-fructose diet + 2% garlic, Group 7 = Standard diet + 2% turmeric; Group 8 = High-fructose diet +2% mixed turmeric:garlic (50% w/w)

Palatability plays important role in the rate at which sweetened diets such as high-fructose diet is consumed thereby altering the hunger and satiety homeostasis (Lindqvist et al., 2008). Two important diet regulatory hormones insulin and leptin necessary for the metabolism of energy molecules are not elicited following the intake of fructose-rich diets (Arslan & Şanlıer, 2016; Lustig, 2010). Instead, ghrelin, a hormone that promotes overfeeding is increased following fructose consumption (Teff et al., 2004). Furthermore, fructose is a source of unregulated production of acetyl-CoA used in hepatic de novo lipogenesis (Samuel, 2011; Taskinen et al., 2017). High-fructose consumption has also been associated with obesity and other metabolic diseases (Hannou et al., 2018; Malik et al., 2019) which are mainly due to an uncontrolled supply of acetyl-CoA intermediates. Moreover, fructose has also been shown to induce the synthesis of enzymes required for the synthesis of fatty acids (Softic et al., 2017) and stimulate sterol regulatory element–binding protein 1c (SREBP1c) and carbohydrate-responsive element–binding protein (ChREBP) (Herman & Samuel, 2016) even in the absence of insulin which are both regulators of de novo lipogenesis (Ramos et al., 2017). ChREBP is activated by glucose while SREBP-1c is activated by insulin and both respectively upregulate gene expressions of glycolytic and lipogenic enzymes particularly in the liver (Linden et al., 2018).

Our results show that the inclusion of garlic and/or turmeric in the diets could antagonize the effects of fructose on feed intake and weight gain and this probably explains the relative weight decrease observed in the groups fed high-fructose diets supplemented with garlic and/or ginger. Lai et al. (2014) report that garlic up-regulates lipolytic genes and down-regulates sterol regulatory element-

binding protein-1c (SREBP1c), a lipogenic gene while curcumin, the main bioactive component of turmeric was found to inhibit (SREBP) expression (Vafaeipour et al., 2022). In another study with mice, garlic administration was shown to have stimulatory effects on AMP-activated protein kinase (AMPK) and decreased gene expressions of adipogenesis leading to decreased body weight gain and epididymal fat accumulation (Kim & Kim, 2011). AMPK balances nutrient supply with energy demand. Furthermore, Lee et al. (2011) reported that dietary supplementation with garlic decreases the expression of genes for adipogenesis and stimulates the expression of UCP in mice with high-fat diet-induced obesity which resulted in a decreased mass of the adipose tissue. Besides the direct weight-reducing effects of garlic, garlic stimulates the secretion of norepinephrine thereby enhancing triglyceride catabolism and thermogenesis (Oi et al., 1999).

Table 4. Lipid profile and atherogenic indices of rats fed garlic and/or turmeric supplemented high-fructose diets

Group	Total cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
G1	97.67 ± 0.88^{bc}	52.00 ± 0.73^{b}	20.00 ± 1.15^{bc}	67.27 ± 1.70^{bc}
G2	132.33 ± 1.45^{f}	82.67 ± 0.67^{d}	15.33 ± 0.88^{a}	100.47 ± 1.39^{e}
G3	89.00 ± 1.00^{a}	46.00 ± 0.00^{a}	23.00 ± 1.00^{c}	56.80 ± 0.00^{a}
G4	101.33 ± 2.40^{c}	51.67 ± 2.03^{b}	23.67 ± 0.88^{c}	67.33 ± 1.68^{bc}
G5	109.00 ± 1.00^{d}	60.50 ± 2.50^{c}	28.50 ± 1.50^{d}	68.40 ± 1.00^{c}
G6	118.67 ± 0.67^{e}	61.00 ± 1.00^{c}	30.00 ± 1.73^{d}	76.67 ± 2.18^{d}
G7	114.00 ± 3.06^{d}	81.67 ± 0.88^{d}	16.67 ± 0.67^{ab}	81.00 ± 2.34^{d}
G8	93.00 ± 3.02^{ab}	54.67 ± 1.33^{b}	20.00 ± 1.15^{bc}	73.37 ± 0.81^{ab}

Values are presented as mean ± SEM for 3 determinations. Values with different superscripts along the same column are significantly different ($p < 0.05$). HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, Group 1 = Standard diet (normal control), Group 2 = High-fructose diet (positive control), Group 3 = High-fructose diet + 2% turmeric, Group 4 = Standard diet + 2% garlic, Group 5 = Standard diet + 2% mixed turmeric:garlic (50% w/w), Group 6 = High-fructose diet + 2% garlic, Group 7 = Standard diet + 2% turmeric; Group 8 = High-fructose diet +2% mixed turmeric:garlic (50% w/w)

Table 5. Atherogenic and coronary risk indices of rats fed garlic and/or turmeric supplemented high-fructose diets

Group	Atherogenic index	Coronary risk index
G1	3.40 ± 0.28^{a}	4.92 ± 0.31^{b}
G2	6.60 ± 0.40^{c}	8.68 ± 0.47^{d}
G3	2.47 ± 0.11^{a}	3.88 ± 0.13^{a}
G4	2.85 ± 0.09^{a}	4.29 ± 0.09^{ab}
G5	2.41 ± 0.16^{a}	3.83 ± 0.17^{a}
G6	2.57 ± 0.22^{a}	3.98 ± 0.25^{a}
G7	4.86 ± 0.06^{b}	6.85 ± 0.10^{c}
G8	3.12 ± 0.17^{a}	4.67 ± 0.20^{ab}

Values are presented as mean ± SEM for 3 determinations. Values with different superscripts along the same column are significantly different ($p < 0.05$). HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, Group 1 = Standard diet (normal control), Group 2 = High-fructose diet (positive control), Group 3 = High-fructose diet + 2% turmeric, Group 4 = Standard diet + 2% garlic, Group 5 = Standard diet + 2% mixed turmeric:garlic (50% w/w), Group 6 = High-fructose diet + 2% garlic, Group 7 = Standard diet + 2% turmeric; Group 8 = High-fructose diet +2% mixed turmeric:garlic (50% w/w)

Curcumin has also been shown to have anti-obesity activities by inducing apoptosis of 3T3-L1 adipocytes, inhibiting adipogenesis, and activating lipolysis (Wu et al., 2019). According to Kang and Kim (2010), curcumin decreases glucose levels by inhibiting glucose-6-phosphatase and phosphoenolpyruvate carboxykinase and thus activates glycolytic and glycogenic pathways while downregulating gluconeogenesis. Curcumin has also been reported to stimulate insulin production in hyperglycemic individuals to maintain a euglycemic state (Na et al., 2011). Also, curcumin increases adiponectin release and lowers the levels of pro-inflammatory interleukin (IL)-6 IL-1β and tumor necrosis factor-α in patients with type 2 diabetes mellitus.

As observed in this study, the improved insulin sensitivity in the groups fed high-fructose diets supplemented with garlic and/or turmeric (Table 3) could partly be due to the anti-obesity activities of the spices. Insulin resistance is usually associated with an increase in body weight in several ways including the interference with inefficient energy utilization arising from a surplus supply of high-energy molecules (Samuel & Shulman, 2016), interference with insulin signaling by toxic metabolites formed from ectopic deposits of lipids (Lee et al., 2011) or triggering of inflammation which could inhibit insulin receptor substrate 1 (IRS-1) and insulin receptor (IR) in the insulin signal transduction pathway (Ye & Gimble, 2011). Therefore, by regulating energy intake and weight gain as discussed, the inclusion of these spices could protect against insulin resistance. From our results, the inclusion of garlic and/or turmeric powder in the diets probably mediates weight control and insulin sensitivities in high-fat diet-exposed Wistar rats.

3.2. Lipid profiles and atherogenic indices of rats fed garlic and/or turmeric-supplemented high-fructose diets

Table 4 shows the lipid profile and atherogenic indices of rats fed garlic and/or turmeric-supplemented high-fructose diet. Except for the high-fructose diet + 2% mixed turmeric:garlic group (G8), the lipid profiles of all other groups were elevated ($p < 0.05$) when compared with the normal control group (G1). However, the lipid profiles of all the high-fructose diet groups that received supplements had significantly ($p < 0.05$) lower serum total cholesterol, triglycerides, and LDL-C and significantly ($p < 0.05$) higher HDL when compared with the positive control (G2). Interestingly, total cholesterol, serum triglycerides, HDL, and LDL levels of the group fed a 2% turmeric-supplemented normal diet did not differ significantly ($p > 0.05$) from that of the normal control group (G1).

As shown in Table 5, there is an elevated coronary risk in the group fed a high-fructose diet only (positive control group). The atherogenic index of groups that received supplemented high-fructose diets was comparable to the normal control group ($p < 0.05$) but significantly different ($p < 0.05$) from the positive control group (G2). Except for the positive control group (G2), the group fed a turmeric-supplemented normal diet (G7) had significantly higher AI and CRI compared with the other experimental groups.

As results indicate improvements in weight, blood glucose levels, and reduced likelihood for insulin resistance in the groups of rats fed garlic and/or turmeric-supplemented diets, the anti-dyslipidemic

traits observed in Table 5 for the treatment groups are quite expected. Dyslipidemia is an independent risk factor component of metabolic syndrome for atherosclerotic patients (Ginsberg et al., 2006). In insulin resistance, for example, there is poor VLDL clearance due to a decrease in lipoprotein lipase (LPL) mRNA expression (Rashid et al., 2003). Fructose metabolism supplies abundant triose-phosphates which are the precursors of both glycerol- and the fatty-acyl moieties of VLDL-triglycerides. Furthermore, stimulation of SREBP by fructose activates HMG-CoA reductase and fatty acid synthase (FAS) which play important roles in cholesterol and fatty acid biosynthesis respectively. The observed anti-dyslipidemic effect of turmeric and/or garlic supplementation in a high-fructose diet is consistent with reported anti-cardiometabolic functions as well as the cardioprotective role of curcuminoids (Johnston et al., 2017; Qin et al., 2017). In another study, garlic and its bioactive component, allicin have been shown to also decrease the HMG-CoA reductase activity and the expression of HMG-CoA reductase mRNA in rats with hypercholesterolemia (Gupta & Porter, 2001; Rai et al., 2009). LXR-α is a lipogenic transcription factor that causes the induction of SREBP-1c. Garlic and turmeric as reported by Mohammadi and Oshaghi (2014) inhibit LXR-α expression in the liver but stimulate LXR-α expression in the intestine. Decreasing LXR-α expression in the liver will decrease SREBP1c and therefore decrease the expression of lipogenic enzymes like ACC and FAS as earlier discussed. On the other hand, by stimulating LXR-α in the intestine, garlic reduces intestinal absorption of cholesterol. Sahebkar et al. (2014) also noted that curcumin decreases lipogenic gene expressions in diet-induced metabolic syndrome and therefore, is a regulator of plasma lipid concentration. Besides decreasing the hepatic expression of lipogenic transcription factors LXR-α and SREBP1c (Maithilikarpagaselvi et al., 2016), curcumin has also been reported to covalently modify FAS by competitively binding to malonyl/acetyltransferase domain resulting in decreased TAG synthesis. Our results suggest the long-term consumption of diets supplemented with turmeric and/or garlic could prevent dyslipidemia and thus reduce cardiometabolic risks associated with excessive consumption of metabolic syndrome-causing diets.

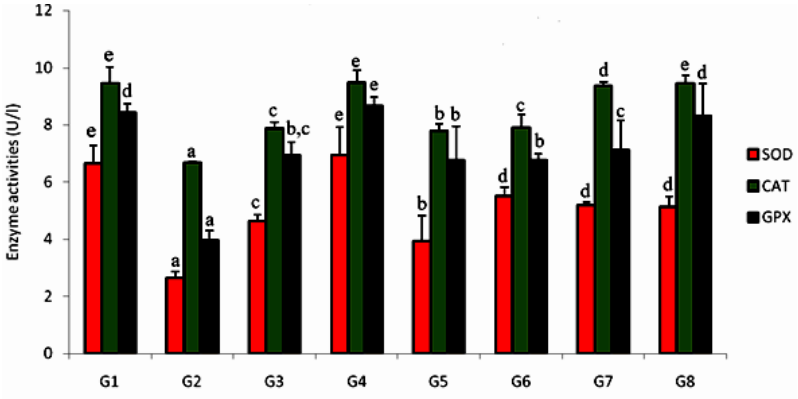

Figure 1. Serum antioxidant enzymes activities in rats fed high-fructose diets supplemented with garlic and/or turmeric

Values are presented as mean ± SEM. Columns with different superscripts for a given enzyme are significantly different ($p < 0.05$). SOD = Superoxide dismutase, CAT = Catalase, GPx = Glutathione peroxidase, G1 = Standard diet (normal control), G2 = High-fructose diet (positive control), G3 = High-fructose diet + 2% turmeric, G4 = Standard diet + 2% garlic, G5 = Standard diet + 2% mixed turmeric:garlic (50% w/w), G6 = High-fructose diet + 2% garlic, G7 = Standard diet + 2% turmeric; G8 = High-fructose diet +2% mixed turmeric:garlic (50% w/w)

3.3. Activities of antioxidant enzymes in rats fed garlic and/or turmeric-supplemented high-fructose diets

Figure 1 presents the activities of serum antioxidant enzymes of rats fed a high-fructose diet supplemented with garlic and/or turmeric. The serum enzyme activities of all the studied antioxidant enzymes (SOD, catalase, and glutathione peroxidase) were significantly higher in all groups fed garlic and/or turmeric-supplemented diets as compared with the positive control group, but mostly lower than the activities in the normal control (Figure 1).

Oxidative stress is an important component of metabolic syndrome and thus a risk factor for the development of cardiometabolic diseases. Imam et al. (2022) noted in their study that intake of high-fructose diets results in hyperglycemia and insulin resistance - two leading causes of oxidative stress. Thus excess energy-rich substrates in the metabolic pool especially in obese individuals increase the likelihood of excess production of free radicals (McMurray et al., 2016). The elevated activities of the antioxidant enzymes are consistent with the observed changes in body weight, and reduced risks of insulin resistance and dyslipidemia in the groups fed a high-fructose diet supplemented with garlic and/or turmeric. Oxidative stress is not only a major pathogenesis of these conditions, it is further exacerbated by the conditions (Maslov et al., 2019). In our previous report (Idoko et al., 2022), it was suggested that the hepatoprotective and nephroprotective effects of these supplements may also have a balancing effect on oxidative redox. Earlier reports (Afrin et al., 2017; Coban et al., 2012) demonstrated that curcumin lowers the production of free radicals and stimulates the synthesis of antioxidant enzymes. Similarly, allicin was found to increase concentrations of glutathione in the liver (Panyod & Sheen, 2020). Therefore findings in this study and earlier reports suggest the inclusion of the spices may not only retard conditions that lead to oxidative stress but also directly scavenge free radicals. Our finding strongly suggests that the inclusion of garlic and/or turmeric in high-fructose diets improved the oxidative status exhibited by experimental rats that received supplementation.

4. Conclusions

In conclusion, our results reveal that the inclusion of garlic and/or turmeric powder in a metabolic syndrome-causing diet was beneficial in improving the atherogenic and coronary risk indices, as well as the HOMA-IR of experimental rats that received supplementation, and this could prevent long-term excess fat accumulation, dyslipidemia, and oxidative stress. Thus, the inclusion of garlic and/or turmeric powder in the diet may forestall the development of the physical and biochemical components of metabolic syndrome risk factors which were maintained on a high-fructose diet for 8 weeks in rats.

Acknowledgments

None.

Conflict of interest

The authors confirm that there are no known conflicts of interest.

Statement of ethics

The rats were kept according to the standards for keeping experimental rodents as approved by the Federal University Dutsin-Ma Ethical Committee on the use of experimental animals and human subjects (FUDMA/IEC/2021205).

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Funding

None.

CRediT authorship contribution statement

Ali Siddiq Idoko: Conceptualization and interpretation of data, Writing original draft
Aliyu Abdullahi: Methodology, Formal analysis
Masud Eneji Sadiq: Literature review, Formal analysis, Proofreading
Bilkis Muhammad Maibalangu: Experimental investigation, Data collection

ORCID Numbers of the Authors

A. S. Idoko: 0000-0003-1700-7631
A. Abdullahi: 0000-0002-4020-0459
M. E. Sadiq: 0000-0001-5193-4338
B. M. Maibalangu: 0000-0003-3781-7682

Supplementary File

None.

Publisher's Note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

Afrin, R., Arumugam, S., Rahman, A., Wahed, M. I. I., Karuppagounder, V., Harima, M., Suzuki, H., Miyashita, S., Suzuki, K., *et al.* (2017). Curcumin ameliorates liver damage and progression of NASH in NASH-HCC mouse model possibly by modulating HMGB1-NF-κB translocation. *International Immunopharmacology, 44*, 174-182.

Alberti, K. G., Eckel, R. H., Grundy, S. M., Zimmet, P. Z., Cleeman, J. I., Donato, K. A., Fruchart, J. C., James, W. P. T., Loria, C. M., *et al.* (2009). Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. *Circulation, 120*(16), 1640-1645.

Anand, P., Kunnumakkara, A. B., Newman, R. A., & Aggarwal, B. B. (2007). Bioavailability of curcumin: problems and promises. *Molecular Pharmaceutics, 4*(6), 807-818.

Arslan, S., & Şanlıer, N. (2016). Relationship between daily dietary fructose intake, body composition and biochemical parameters patients with type 2 diabetes. *Journal of Human Sciences, 13*(2), 2642-2655.

Coban, D., Milenkovic, D., Chanet, A., Khallou-Laschet, J., Sabbe, L., Palagani, A., Vanden Berghe, W., Mazur, A., & Morand, C. (2012). Dietary curcumin inhibits atherosclerosis by affecting the expression of genes involved in leukocyte adhesion and transendothelial migration. *Molecular Nutrition & Food Research, 56*(8), 1270-1281.

National Research Council (2011). Guide for the care and use of laboratory animals, National Academies Press. *Washington, DC.*

do Vale Moreira, N. C., Hussain, A., Bhowmik, B., Mdala, I., Siddiquee, T., Fernandes, V. O., Júnior, R. M. M., & Meyer, H. E. (2020). Prevalence of metabolic syndrome by different definitions, and its association with type 2 diabetes, pre-diabetes, and cardiovascular disease risk in Brazil. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 14*(5), 1217-1224.

Engin, A. (2017). The definition and prevalence of obesity and metabolic syndrome. Obesity and Lipotoxicity. *Advances in Experimental Medicine and Biology,* (Vol. 960): Springer, Cham.

Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry, 18*(6), 499-502.

Gierach, M., Gierach, J., Ewertowska, M., Arndt, A., & Junik, R. (2014). Correlation between body mass index and waist circumference in patients with metabolic syndrome. *International Scholarly Research Notices, 2014*, 514589.

Ginsberg, H. N., Zhang, Y. L., & Hernandez-Ono, A. (2006). Metabolic syndrome: focus on dyslipidemia. *Obesity, 14*(2S), 41S-49S.

Gupta, N., & Porter, T. D. (2001). Garlic and garlic-derived compounds inhibit human squalene monooxygenase. *The Journal of Nutrition, 131*(6), 1662-1667.

Hannou, S. A., Haslam, D. E., McKeown, N. M., & Herman, M. A. (2018). Fructose metabolism and metabolic disease. *The Journal of Clinical Investigation, 128*(2), 545-555.

Herman, M. A., & Samuel, V. T. (2016). The sweet path to metabolic demise: fructose and lipid synthesis. *Trends in Endocrinology & Metabolism, 27*(10), 719-730.

Huang, C. J., McAllister, M. J., Slusher, A. L., Webb, H. E., Mock, J. T., & Acevedo, E. O. (2015). Obesity-related oxidative stress: the impact of physical activity and diet manipulation. *Sports Medicine-Open, 1*(1), 32.

Idoko, A., Abdullahi, A., Maibulangu, B., Nura, L., Imam, N., Bonomi, Z., Muhammed, F., & Umar, S. (2022). *Allium sativum* and *Curcuma longa* Powder Protect Against Hepatotoxic and Nephrotoxic Effects of High-fructose Diet. *FUOYE Journal of Pure and Applied Sciences (FJPAS), 7*(1), 59-78.

Imam, N., Idoko, A., Osibemhe, M., Lawal, N., & Zaharaddeen, A. (2022). Obesity and Insulin Resistance Components of Metabolic Syndrome Induced by High-fructose Diet in Wistar Rats could be attenuated by Spices-Supplemented Diets. *Journal of Applied Sciences and Environmental Management, 26*(5), 893-901.

Johnston, T., Korolenko, T., Pirro, M., & Sahebkar, A. (2017). Preventing cardiovascular heart disease: Promising nutraceutical and non-nutraceutical treatments for cholesterol management. *Pharmacological Research, 120*, 219-225.

Kang, C., & Kim, E. (2010). Synergistic effect of curcumin and insulin on muscle cell glucose metabolism. *Food and Chemical Toxicology, 48*(8-9), 2366-2373.

Kazemi, T., Hajihosseini, M., Moossavi, M., Hemmati, M., & Ziaee, M. (2018). Cardiovascular risk factors and atherogenic indices in an Iranian population: Birjand East of Iran. *Clinical Medicine Insights: Cardiology, 12*, 1179546818759286.

Kim, M., & Kim, H. (2011). Effect of garlic on high fat induced obesity. *Acta Biologica Hungarica, 62*(3), 244-254.

Lai, Y. S., Chen, W. C., Ho, C. T., Lu, K. H., Lin, S. H., Tseng, H. C., Lin, S. Y., & Sheen, L. Y. (2014). Garlic essential oil protects against obesity-triggered nonalcoholic fatty liver disease through modulation of lipid metabolism and oxidative stress. *Journal of Agricultural and Food Chemistry, 62*(25), 5897-5906.

Lee, M. S., Kim, I. H., Kim, C. T., & Kim, Y. (2011). Reduction of body weight by dietary garlic is associated with an increase in uncoupling protein mRNA expression and activation of AMP-activated protein kinase in diet-induced obese mice. *The Journal of Nutrition, 141*(11), 1947-1953.

Linden, A. G., Li, S., Choi, H. Y., Fang, F., Fukasawa, M., Uyeda, K., Hammer, R. E., Horton, J. D., Engelking, L. J., *et al.* (2018). Interplay between ChREBP and SREBP-1c coordinates postprandial glycolysis and lipogenesis in livers of mice [S]. *Journal of Lipid Research, 59*(3), 475-487.

Lindqvist, A., Baelemans, A., & Erlanson-Albertsson, C. (2008). Effects of sucrose, glucose and fructose on peripheral and central appetite signals. *Regulatory Peptides, 150*(1-3), 26-32.

Lustig, R. H. (2010). Fructose: metabolic, hedonic, and societal parallels with ethanol. *Journal of the American Dietetic Association, 110*(9), 1307-1321.

Maithilikarpagaselvi, N., Sridhar, M. G., Swaminathan, R. P., Sripradha, R., & Badhe, B. (2016). Curcumin inhibits hyperlipidemia and hepatic fat accumulation in high-fructose-fed male Wistar rats. *Pharmaceutical Biology, 54*(12), 2857-2863.

Malik, V. S., Li, Y., Pan, A., De Koning, L., Schernhammer, E., Willett, W. C., & Hu, F. B. (2019). Long-term consumption of sugar-sweetened and artificially sweetened beverages and risk of mortality in US adults. *Circulation, 139*(18), 2113-2125.

Maslov, L. N., Naryzhnaya, N. V., Boshchenko, A. A., Popov, S. V., Ivanov, V. V., & Oeltgen, P. R. (2019). Is oxidative stress of adipocytes a cause or a consequence of the metabolic syndrome? *Journal of Clinical & Translational Endocrinology, 15*, 1-5.

McMurray, F., Patten, D. A., & Harper, M. E. (2016). Reactive oxygen species and oxidative stress in obesity—recent findings and empirical approaches. *Obesity, 24*(11), 2301-2310.

Mohammadi, A., & Oshaghi, E. A. (2014). Effect of garlic on lipid profile and expression of LXR alpha in intestine and liver of hypercholesterolemic mice. *Journal of Diabetes & Metabolic Disorders, 13*, 20.

Na, L. X., Zhang, Y. L., Li, Y., Liu, L. Y., Li, R., Kong, T., & Sun, C. H. (2011). Curcumin improves insulin resistance in skeletal muscle of rats. *Nutrition, Metabolism and Cardiovascular Diseases, 21*(7), 526-533.

Nguyen, N. T., Magno, C. P., Lane, K. T., Hinojosa, M. W., & Lane, J. S. (2008). Association of hypertension, diabetes, dyslipidemia, and metabolic syndrome with obesity: findings from the National Health and Nutrition Examination Survey, 1999 to 2004. *Journal of the American College of Surgeons, 207*(6), 928-934.

Oi, Y., Kawada, T., Shishido, C., Wada, K., Kominato, Y., Nishimura, S., Ariga, T., & Iwai, K. (1999). Allyl-containing sulfides in garlic increase uncoupling protein content in brown adipose tissue, and noradrenaline and adrenaline secretion in rats. *The Journal of Nutrition, 129*(2), 336-342.

Panyod, S., & Sheen, L. Y. (2020). Beneficial effects of Chinese herbs in the treatment of fatty liver diseases. *Journal of Traditional and Complementary Medicine, 10*(3), 260-267.

Pekgor, S., Duran, C., Berberoglu, U., & Eryilmaz, M. A. (2019). The role of visceral adiposity index levels in predicting the presence of metabolic syndrome and insulin resistance in overweight and obese patients. *Metabolic Syndrome and Related Disorders, 17*(5), 296-302.

Qin, S., Huang, L., Gong, J., Shen, S., Huang, J., Ren, H., & Hu, H. (2017). Efficacy and safety of turmeric and curcumin in lowering blood lipid levels in patients with cardiovascular risk factors: a meta-analysis of randomized controlled trials. *Nutrition Journal, 16*, 68.

Rai, S. K., Sharma, M., & Tiwari, M. (2009). Inhibitory effect of novel diallyldisulfide analogs on HMG-CoA reductase expression in hypercholesterolemic rats: CREB as a potential upstream target. *Life Sciences, 85*(5-6), 211-219.

Ramos, V. W., Batista, L. O., & Albuquerque, K. T. (2017). Effects of fructose consumption on food intake and biochemical and body parameters in Wistar rats. *Revista Portuguesa de Cardiologia (English Edition), 36*(12), 937-941.

Rashid, S., Watanabe, T., Sakaue, T., & Lewis, G. F. (2003). Mechanisms of HDL lowering in insulin resistant, hypertriglyceridemic states: the combined effect of HDL triglyceride enrichment and elevated hepatic lipase activity. *Clinical Biochemistry, 36*(6), 421-429.

Rehman, K., & Akash, M. S. H. (2016). Mechanisms of inflammatory responses and development of insulin resistance: how are they interlinked? *Journal of Biomedical Science, 23*, 87.

Rodriguez-Cano, A., Mier-Cabrera, J., Balas-Nakash, M., Muñoz-Manrique, C., Legorreta-Legorreta, J., & Perichart-Perera, O. (2015). Dietary changes associated with improvement of metabolic syndrome components in postmenopausal women receiving two different nutrition interventions. *Menopause (New York, NY), 22*(7), 758-764.

Sahebkar, A., Chew, G. T., & Watts, G. F. (2014). Recent advances in pharmacotherapy for hypertriglyceridemia. *Progress in Lipid Research, 56*, 47-66.

Samuel, V. T. (2011). Fructose induced lipogenesis: from sugar to fat to insulin resistance. *Trends in Endocrinology & Metabolism, 22*(2), 60-65.

Samuel, V. T., & Shulman, G. I. (2016). The pathogenesis of insulin resistance: integrating signaling pathways and substrate flux. *The Journal of Clinical Investigation, 126*(1), 12-22.

Softic, S., Gupta, M. K., Wang, G. X., Fujisaka, S., O'Neill, B. T., Rao, T. N., Willoughby, J., Harbison, C., Fitzgerald, K., *et al.* (2017). Divergent effects of glucose and fructose on hepatic lipogenesis and insulin signaling. *The Journal of Clinical Investigation, 127*(11), 4059-4074.

Sperling, L. S., Mechanick, J. I., Neeland, I. J., Herrick, C. J., Després, J. P., Ndumele, C. E., Vijayaraghavan, K., Handelsman, Y., Puckrein, G. A., *et al.* (2015). The cardiometabolic health alliance: working toward a new care model for the metabolic syndrome. *Journal of the American College of Cardiology, 66*(9), 1050-1067.

Taskinen, M. R., Söderlund, S., Bogl, L., Hakkarainen, A., Matikainen, N., Pietiläinen, K., Räsänen, S., Lundbom, N., Björnson, E., *et al.* (2017). Adverse effects of fructose on cardiometabolic risk factors and hepatic lipid metabolism in subjects with abdominal obesity. *Journal of Internal Medicine, 282*(2), 187-201.

Teff, K. L., Elliott, S. S., Tschöp, M., Kieffer, T. J., Rader, D., Heiman, M., Townsend, R. R., Keim, N. L., D'alessio, D., *et al.* (2004). Dietary fructose reduces circulating insulin and leptin, attenuates postprandial suppression of ghrelin, and increases triglycerides in women. *The Journal of Clinical Endocrinology & Metabolism, 89*(6), 2963-2972.

Tian, Y., Su, L., Wang, J., Duan, X., & Jiang, X. (2018). Fruit and vegetable consumption and risk of the metabolic syndrome: A meta-analysis. *Public Health Nutrition, 21*(4), 756-765.

Tune, J. D., Goodwill, A. G., Sassoon, D. J., & Mather, K. J. (2017). Cardiovascular consequences of metabolic syndrome. *Translational Research, 183*, 57-70.

Vafaeipour, Z., Razavi, B. M., & Hosseinzadeh, H. (2022). Effects of turmeric (*Curcuma longa*) and its constituent (curcumin) on the metabolic syndrome: An updated review. *Journal of Integrative Medicine, 20*(3), 193-203.

Wu, L. Y., Chen, C. W., Chen, L. K., Chou, H. Y., Chang, C. L., & Juan, C. C. (2019). Curcumin attenuates adipogenesis by inducing preadipocyte apoptosis and inhibiting adipocyte differentiation. *Nutrients, 11*(10), 2307.

Ye, J., & Gimble, J. M. (2011). Regulation of stem cell differentiation in adipose tissue by chronic inflammation. *Clinical and Experimental Pharmacology and Physiology, 38*(12), 872-878.

Yin, J., Li, M., Xu, L., Wang, Y., Cheng, H., Zhao, X., & Mi, J. (2013). Insulin resistance determined by Homeostasis Model Assessment (HOMA) and associations with metabolic syndrome among Chinese children and teenagers. *Diabetology & Metabolic Syndrome, 5*, 71.