Advances in Bioresearch
Adv. Biores., Vol 13 (2) March 2022: 175-183
©2022 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.13.2.175183

Advances in Bioresearch

ORIGINAL ARTICLE

Olive leaves tea and Apple Cider Vinegar with Lifestyle modification: Potential Effects on Metabolic Syndrome in elderly

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ABSTRACT
This study aims to know the effect of olive leaves and apple cider vinegar on elderly people with metabolic syndrome. Olive leaves tea and apple cider vinegar were first analyzed to find out the antioxidant contents (total polyphenolic and flavonoid) and antioxidant activity (DPPH). In vivo study on elderly people male and female was conducted. The patients were divided into three groups, the first group affected by metabolic syndrome, the second group was given a tea of olive leaves, and the third group was given a tea of olive leaves plus apple cider vinegar with lifestyle modifications for all groups for a period of 12 weeks. The results showed that the polyphenolic content in olive leaves tea and apple cider vinegar were185.02 ± 8.20 and 150.32± 5.16 mg /kg, flavonoid content was 85.02 ± 3.20 and42:93 ± 2.14mg /kg, and Free radical IC_{50} olive leaves tea and apple cider vinegar scavenging activity (DPPH) were 0.85± 0.30 and 0.74 ± 0.24 µL/mL. Olive leaves tea(group II) and olive leaves plus apple cider (group III)showed a significant reduction in blood pressure body weight, total cholesterol levels, triglycerides, blood glucose, liver function and kidney function. Olive leaves group and olive leaves plus apple cider group alters the indicators related to development of metabolic syndrome, because it has beneficial effects on lipids and glucose profiles and prevents the excess of body weight gain.
Key words: *Olive leaves, apple cider,metabolic syndrome, lipid profile, phenolic compounds.*

Received 22.01.2022 Revised 11.02.2022 Accepted 18.03.222

How to cite this article:
Ahlam, S. Alhajri; Amany, M. Basuny & Sayed, A.Galal. Olive leaves tea and apple cider vinegar with lifestyle modification: Potential Effects on metabolic syndrome in elderly. Adv. Biores. Vol 13 [2] March 2022: 175-183.

INTRODUCTION

The Metabolic Syndrome (MS) is one of the world's most serious health issues. Individuals with this syndrome are more likely to develop diabetes, cardiovascular illnesses (CVDs), and eventually die. It's obvious that genetic, metabolic, and environmental factors all have a part in the disease's occurrence [9, 8, 20]. The most essential portion of this collection is abdominal fat, which is defined as fat deposition in the abdominal fatty tissues. Obese MS patients showed greater metabolic issues and CVDs than MS patients of normal weight [6]. Waist circumference (WC) may potentially be used to predict MS recovery and diabetes prognosis [15]. Hypertension, abdominal obesity, higher triglycerides, decreased high density lipoproteins (HDL-c), and increased glycemia/type 2 diabetes are all symptoms of this metabolic change. MS can be avoided with preventive measures and therapeutic strategies such as changes in lifestyle, such as nutrition interventions and physical activity [4]. The leaves of the olive tree (Olea europaea, Oleaceae) have long been employed in traditional herbal medicine to prevent and treat a variety of ailments, particularly in Mediterranean nations. They include a number of potentially beneficial chemicals with hypoglycemic and hypolipidemic effects [11, 13]. Oleuropein, a natural product of the secoiridoid group, is the most active component in olive leaves. Antioxidant compounds in olive leaves, such as oleuropein, hydroxytyrosol, tyrosol; caffeic acid; and ligstroside, have long been related with the protection of certain diseases [26, 2]. Oleuropein has a wide range of pharmacologic and health-promoting qualities, including antiarrhythmic, spasmolytic, immune-stimulant, cardioprotective, hypotensive, anti-inflammatory, antioxidant, and anti-thrombic activities, according to several research. [19, 25]. Vinegar is a diluted acetic acid solution with the same formula as acetic acid, which contains four

hydrogen atoms, two carbon atoms, and two oxygen atoms [7]**.** Around the world, apple cider vinegar is widely used and valued. Several studies have clearly demonstrated numerous benefits of apple cider vinegar consumption, including glucose-lowering effect in patients with glucose abnormalities [12], improved insulin sensitivity in insulin resistant patients, decreased the glycemic index of carbohydrate food for people with and without diabetes, antihyperlipidemic, hepatoprotective effect [21, 22]**,** and modulation of lipid peroxidation. [5]**.** For many years, apple cider vinegar has been utilized as a natural therapy for diabetes management in several parts of the world. Several mechanisms for the action of glucose metabolisms have been reported, including delayed gastric emptying and enteral absorption, increased glucose utilization, suppression of hepatic glucose production, up-regulation of flow-mediated vasodilation, increased lipolysis and reduced lipogenesis, and insulin secretion facilitation. Other processes mentioned include the facilitation of faecal acid bile excretion, higher energy utilization, and increased satiety. [24]**.** The current study aimed at measuring and confirming the effect of olive leaves tea and apple cider vinegar in humans, and evaluating the safety of using olive leaves tea and apple cider vinegar in treating metabolic syndrome patients. So, this experiment was designed to examine the effect of olive leaves tea and apple cider vinegar on blood glucose tests, blood pressure, lipid profile and a range of related clinical analysis in the designed groups of the participants.

MATERIAL AND METHODS

Source of olive leaves and apple cider vinegar: The ripe olive leaves (*Olea europaea*) Koronakii variety were collected during the pruning process in 2020 year from a farm in Giza governorate. Apple cider vinegar was purchased from a local market. The samples were kept in the fridge (3° C) until it was used for the various experiments carried out in this work.

Source of chemicals: We use the commercially available enzyme kits for measuring T.C., T.G., HDL and other clinical measurements; all chemicals are purchased form (Spectrum Diagnostics, Cairo. Egypt. MDSS GmbH, Schiffgraben 41, 30175 Hannover, Germany.)

Olive leaves tea preparation: For the olive leaves tea preparation, green olive leaves were collected, dried and stored until use. Each dose of olive leaves was cut into small pieces and packed in a bag contains 10-gram dried olive leaves. To be ready for use each tea bag was boiled for 5 to 10 minutes in drinking water.

The Antioxidant Contents of olive leaves tea and apple cider vinegar: The total polyphenolic content in the olive leaves tea apple cider vinegar samples were determined by Folin-Ciocalteu reagent using a method described by [28]**;** the value of total polyphenolic compounds was expressed as milligrams of gallic acid equivalent per 100 mL of sample. Total flavonoid content was determined using the method described by [17]**;** the outcome was expressed as milligrams of quercetin equivalent per 100 mL of sample.

The Antioxidant Activities of olive leaves tea and apple cider vinegar: The scavenging activity of olive leaves tea and apple cider vinegar for the radical 2,2-diphenyl-1-picrylhydrazyl (DPPH) was measured as described by [18]**.** The scavenging activity was estimated based on the percentage of DPPH radical scavenged using the following equation:

$\%\text{Inhibition} = A_0 - A_1 / A_0 \times 10$

A_0 is the absorbance of the control; A_1 is the absorbance of the sample. The IC_{50} DPPH was calculated from the obtained graph of inhibition percentage of radical DPPH.

Experimental design: This was a prospective, observational study. All subjects were selected from Beni Suef Governorate suffering from metabolic syndromes (include dyslipidemia, hypertension, glucose intolerance), with age above 50 years old and classified into 3groups. Group I: control group consists of metabolic syndrome patients without intervention. Group II: includes metabolic syndrome patients taking olive leaves tea. Group III: includes metabolic syndrome patients taking olive leaves tea plus apple cider vinegar. Each group includes 15 subjects (n=15) divided into (male and female) subjects. In the current study, each group was monitored for 12 weeks treatment. In the experiment, the patients of group 2 were given a specific dose of olive leaves tea twice daily with a meal, one in the morning and the other in the evening, with modifying their lifestyle. Group 3 patients were given a specific dose of olive leaves tea plus apple cider twice daily with a meal, one in the morning and the other in the evening, with modifying their lifestyle. Blood pressure was measured at baseline screening and after each week until the end of the study. Body weight, body mass index, abdomen circumference, blood glucose, blood lipids, kidney function tests and liver function tests were also measured at baseline screening, and after 12 weeks of treatment. Adverse effects were observed and if present, recorded during the study.

Biochemical measures: Blood samples were drawn after a fasting of not less than 12 h. Blood samples for the measurement of liver function tests, kidney function tests and lipid profile concentrations were

collected in tubes with no additives and allowed to coagulate at room temperature for 30 min. For fasting blood glucose, blood samples were drawn after a fasting of 6 to 8 h. and then post prandial blood glucose blood samples were drawn after 2 hours of the meal. For HbA1c blood samples were drawn on EDTA tubes. All blood samples were separated by centrifugation (10 min, 3000 rpm) and kept at - 20 °C until they were analyzed. Fasting and post prandial blood glucose, HbA1C, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), UREA, Creatinine, serum total cholesterol (TC), triglyceride (TG), Low density lipoprotein (LDL) and high-density lipoprotein (HDL) were measured by a commercially available mentioned enzyme kit. Weight was measured for patients with no shoes, light clothing, by a scale up to the nearest of 0.5 kg. Height was measured for all the participants in stocking feet using a ruler at the apex of the head. Blood pressure was measured for all subjects using a cuff and analog sphygmomanometer and the patient comfortably seated for 10 minutes before the first measurement. Blood pressure was measured for all participants three times, and the mean of it were recorded.

Statistical analysis: All experimental results are expressed as the mean±standard deviation (SD). One-way analysis of variance (ANOVA) followed by Dunnett's test ($p<0.05$ was considered significant comparing to the untreated group) was performed using SPSS version 16 (USA) to compare the effects of low and high concentration of vinegar (synthetic acetic acid vinegar and Nipa vinegar) treated groups with untreated obesity group for all experiments.

RESULTS AND DISCUSSION

Total Polyphenolic Content, Total Flavonoid Content, and Antioxidant Activities (DPPH): Total Polyphenolic Content, Total Flavonoid Content, and Antioxidant Activities DPPH (IC50) values of olive leaves tea and apple cider vinegar are shown in Table 1 &2. Generally, the total polyphenolic content was 185.02 ± 8.20 and 150.32 ± 5.16 mg /kg, flavonoid content was 85.02 ± 3.20 and 42:93 ± 2.14 mg /kg, and Free radical IC_{50} olive leaves and apple cider vinegar scavenging activity (DPPH) were 0.85 ± 0.30 and 0.74 ± 0.24 µL/mL. Olive leaves tea and Apple cider vinegar is very well known for its unsuspected health benefits; it is rich in bioactive molecules such as polyphenolic compounds and flavonoids known for its several therapeutic effects**.** The results of antioxidant contents obtained in olive leaves tea and apple vinegar are in accordance with those reported by previous reports [13, 14, 1, 2].

Table 1. The Antioxidant Contents of olive leaves tea and apple cider vinegar:

Antioxidant Contents	olive leaves tea	apple cider vinegar
Total polyphenolic (mg/kg)	185.02 ± 8.20	150.32 ± 5.16
Flavonoid (mg/kg)	85.02 ± 3.20	42:93 ± 2.14

Mean value ± standard deviation (SD).

Table 2. The Antioxidant Activities of olive leaves tea and apple cider vinegar:

Antioxidant activities	olive leaves tea	apple cider vinegar
IC_{50} DPPH (µL/mL)	0.85 ± 0.30	0.74 ± 0.24

Mean value ± standard deviation (SD).

Effect of olive leaves tea and apple cider on blood pressure: Blood pressure is measured in millimeters of mercury (mmHg) and is given as 2 numbers: systolic pressure – the pressure when your heart pushes blood out-diastolic pressure – the pressure when your heart rests between beats. 3.34The highest number is always the systolic pressure and it's always given first. For example, a blood pressure given as "120 over 80" or 120/80mmHg means a systolic pressure of 120mmHg and a diastolic pressure of 80mmHg. Figure 1(A&B) shows the change in blood pressure (systolic and diastolic) for the different groups (Group I: metabolic syndrome patients without intervention. Group II: metabolic syndrome patients taking olive leaves tea and Group III metabolic syndrome patients taking olive leaves tea plus apple cider vinegar).The results indicate a significant decrease in blood pressure values (systolic and diastolic) for the group of patients who consumed olive leaves tea with lifestyle modifications (group II) (129.53± 3.34and80.86± 2.01, respectively)compared to the group 1(metabolic syndrome)(156.80± 4.12 and 92.53±2.24, respectively). In the same way, eating olive leaves plus apple cider vinegar with lifestyle modifications (group III) led to a significant decrease in blood pressure values (127.60±3,21and 83.86±2.22, respectively) compared to the group 1. The results of blood pressure obtained in olive leaves tea and apple cider vinegar are in accordance with [2, 23].

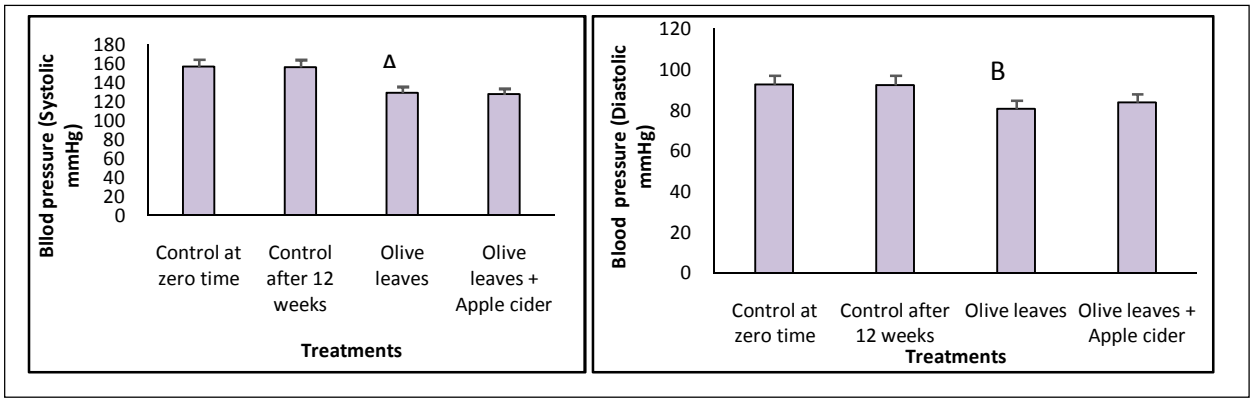

Fig 1: Effect of olive leaves tea and apple cider on blood pressure

Effect of olive leaves tea and apple cider vinegar on blood sugar: Oxidation of glucose present in the peripheral blood represents the major source of cellular energy in the body. Dietary glucose is stored in the liver in the form of glycogen or converted to fatty acids and stored in the adipose tissues. The accurate estimation of glucose is important in the diagnosis and management of hyperglycemia & hypoglycemia. The most frequent cause of hyperglycemia is diabetes mellitus resulting from a deficiency in insulin secretion or action. Hypoglycemia may be the result of an insulinoma, insulin administration, inborn error of carbohydrate metabolism or fasting. The results indicate a significant decrease in the fasting blood glucose level (F. BL. G.) in both group II who consumed olive leaves tea with lifestyle modification (111.73± 2.91) and group III who consumed olive leaves tea plus apple cider vinegar with lifestyle modification (106.00±1.86) compared to group 1 metabolic syndrome patients (174.53±4.32) (Figure 2 A).

Concurrently, there was a significant difference in postprandial blood glucose (PP. BL. G.) in group II (143.46±3.33)and group III(139.13± 3.06) compared to group 1(224.26±6.34)(Figure 2B).

After 12 weeks of treatment, there was a significant increase in glycosylated hemoglobin (HbA1c.) in the group of patients who took olive leaves tea with lifestyle modification (7.26±0.12) and also in the group of patients who took olive leaves tea plus apple cider vinegar with lifestyle modification (7.10± 0.11) compared with group 1(9.93±0.22) (Figure 2 C). Glycosylated hemoglobin is formed continuously by the abduction of glucose by co-valent bonding to the amino terminal valine of the hemoglobin beta chain progressively & irreversibly over a period of time & is stable till the life of the RBC. This process is slow, non-enzymatic and is dependent on the average blood Glucose concentration over a period of time. These results are consistent with the prophetic medicine. The Prophet Muhammad, may God's prayers and peace be upon him, recommended drinking vinegar in the hadith: "vinegar is the best edible." Moreover, the apple vinegar has been shown to reduce fasting blood glucose by reducing the post-prandial insulin response [23].

Effect of olive leaves tea and apple cider vinegar on Lipid profile: Lipid profile levels showed a decrease in its values during the course of the experiment in the three groups (Figure 3). Data in Figure 3shows the change in lipid profile (mg/dl) and contains A: The change in total cholesterol (mg/dl), B: The change in triglycerides (mg/dl), C: The change in high-density lipoprotein (mg/dl) and D: The change in low-density lipoprotein (mg/dl) during the study.With the more pronounced effects than on blood pressure, olive leaves tea (group II) and olive leaves tea plus apple cider vinegar(group III) intake was also associated with an improvement in lipid profile with a significant physiologically reductions in total cholesterol (195.20± 4.71 and 195.13± 4,22, respectively), Low-density lipoprotein cholesterol (118.85± 2.13 and117.63± 2.49, respectively) and triglycerides(129.06±3.11 and 129.86± 3.32, respectively) compared with metabolic syndrome patients (group 1) (249.80 ± 6.12 ,162.61± 4.10 and 210.93±5.42, respectively) and increase in high density lipoprotein cholesterol (50.53± 0.53 and 50.13± 0.50, respectively) in group II and III compared with group 1(45.00±0.32). The finding results revealed that olive leaves tea and apple cider vinegar was able to reduce moderately the concentration of total cholesterol in patients as well as triglycerides and low-density lipoprotein cholesterol in patients of both sexes. In opposite, it increased the level of high-density lipoprotein cholesterol in male and female patients. Results are in agreement with previous studies which have shown that the olive leaves tea and apple cider vinegar with lifestyle modification modulates the lipid profile [10, 27, 2].

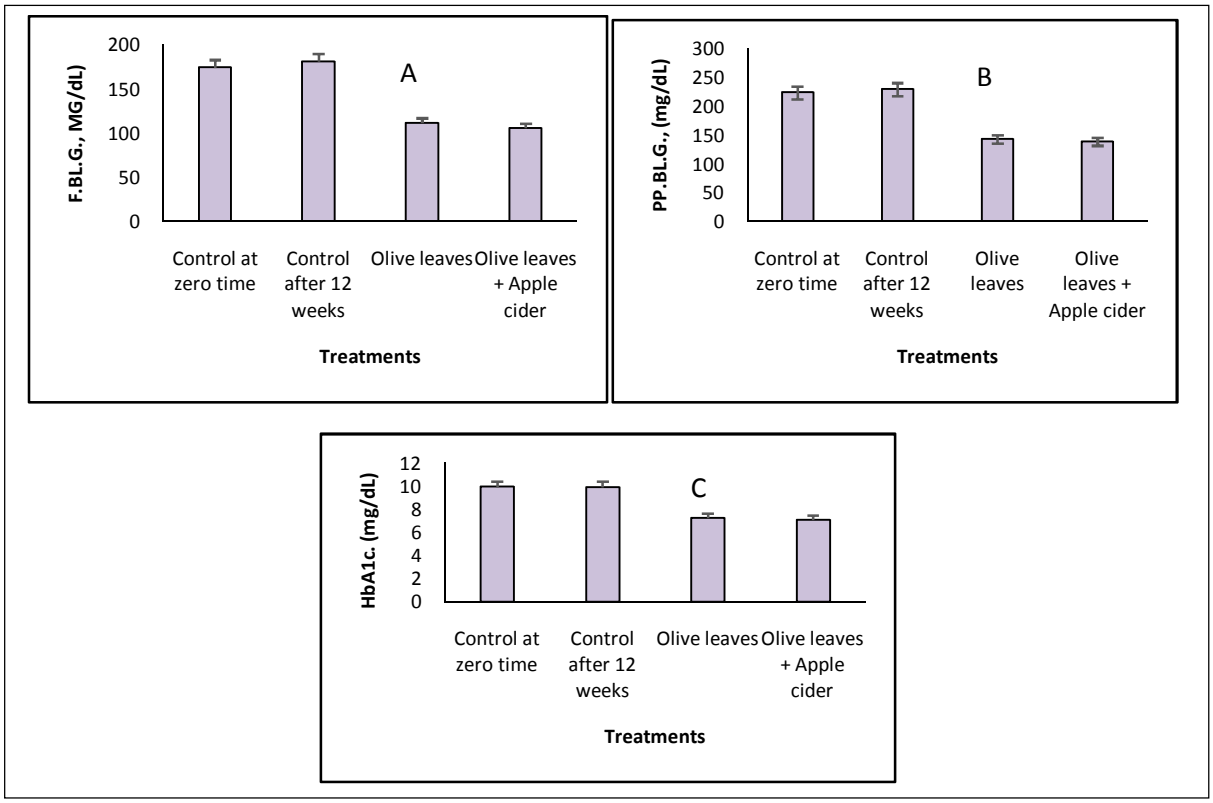

Fig 2: Effect of olive leaves tea and apple cider vinegar on blood sugar

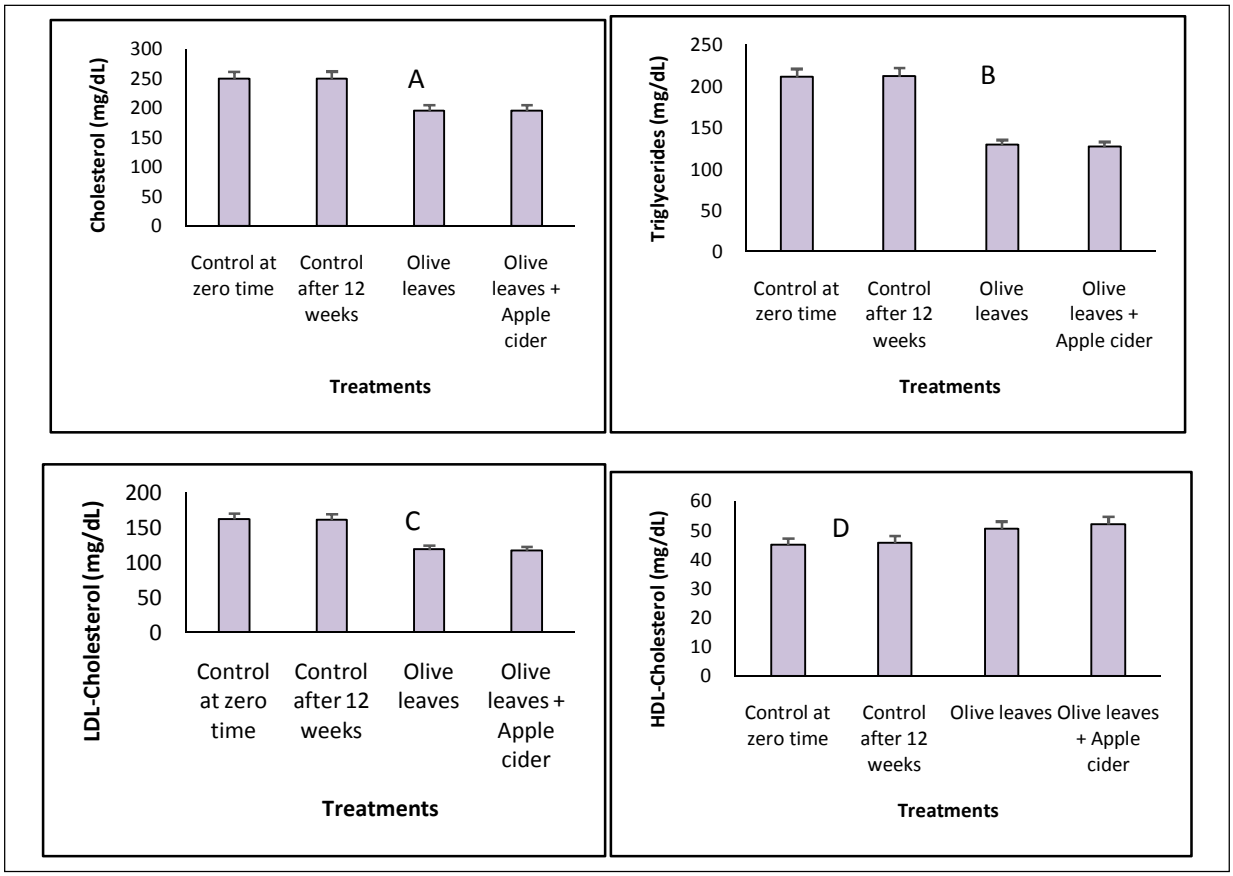

Fig 3: Effect of olive leaves tea and apple cider vinegar on Lipid profile

Effect of olive leaves tea and apple cider vinegar on Liver function tests: Figure 4 divided into **A:** The change in Alanine aminotransferase: (The difference was 39.33±0.41, 25.33± 0.31, and29.46 ± 0.22 U/L for groups 1, II and III respectively) and **B:** The change in Aspartate aminotransferase: (The difference was 43.33± 0.45,24.13±0.23and 30.10±0.20 U/L for group 1, II and III respectively).
Good improvement in the liver functions had noticed in the group II (olive leaves tea)and III (olive leaves tea plus apple cider vinegar) compared with group 1(metabolic syndrome). There is a significant decrease in the studied groups for the two liver function tests, and this verify the results of other studies mentioned that, oleuropein and rutin decreased body weight gain and improved plasma lipid profiles and hepatic steatosis in HFD-fed mice [16]**.** These results were in agreement with previous studies [11, 21]**.**

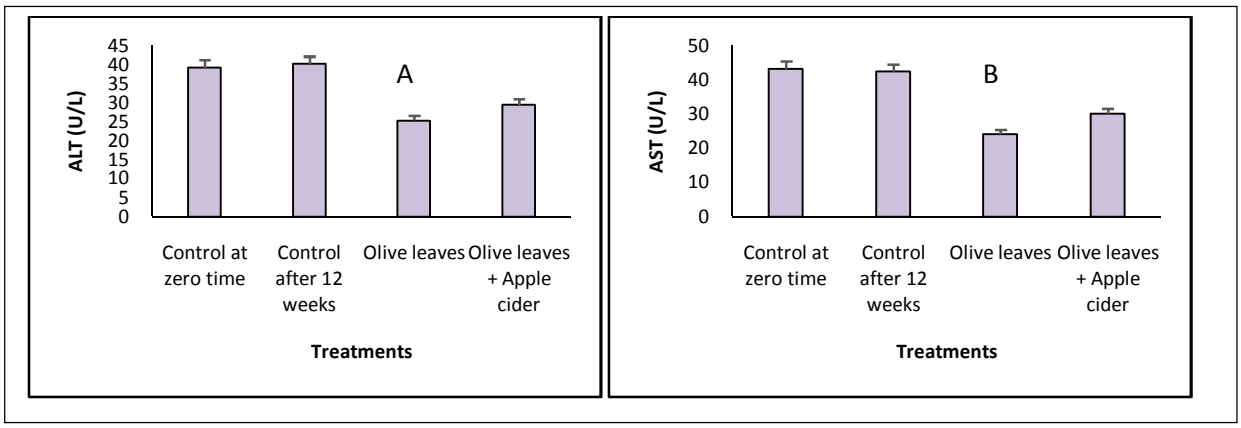

Fig 4: Effect of olive leaves tea and apple cider vinegar on Liver function tests

Effect of olive leaves decoction on Kidney function tests: Creatine is synthesized in kidney, liver and pancreas. It is transported in blood to other organs such as muscle and brain where it is phosphorylated to phosphocreatine. Some free creatine in muscle is converted to creatinine daily and the amount of creatinine produced is proportional to muscle mass. In the absence of renal disease, excretion rate of creatinine in an individual is relatively constant. However, serum urea levels may be affected by dehydration, diet and protein metabolism [3]**.**
Figure 5 consists of **A:** The change in Urea: (the difference was 44.06±0.51, 31.06±0.33, and33.46±0.34mg/dL for group 1,II and III respectively) and **B:** The change in Creatinine: (the difference was 1.53±0.10,0.99± 0.01 and 1.08±0.11mg/dL for group I,II and III respectively) during this study. There is an improvement in the kidney function tests had noticed in the groupsII(olive leaves tea)and III(olive leaves tea plus apple cider vinegar) compared with group 1 (metabolic syndrome). This effect could be due to its phenolic components particularly; oleuropeinpyrogallol and catechin .Ousaaid *et al.,* [23] reported that oleuropein, catechin and pyrogallol can prevent kidney damage and lower the levels of creatinemia and uricemia**.**

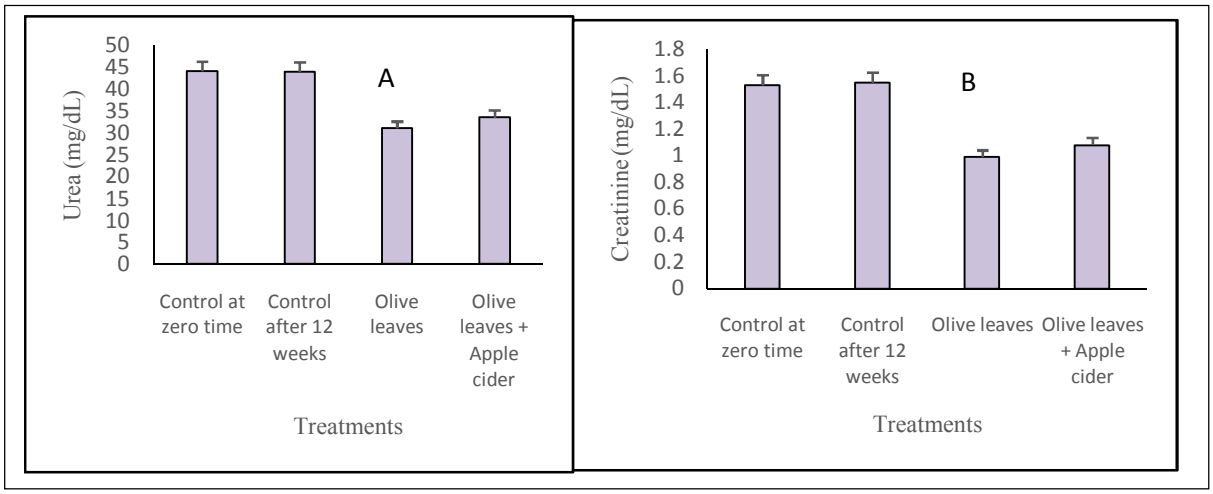

Fig 5 : Effect of olive leaves decoction on Kidney function tests

Effect of olive leaves decoction on body measurements: Body Mass Index is a simple calculation using a person's height and weight. The formula is BMI = kg/m2 where kg is a person's weight in kilograms and m2 is their height in meters squared. A BMI of 25.0 or more is overweight, while the healthy range is 18.5 to 24.9. BMI applies to most adults 18-65 years.

A significant improvement in the body measurements occurred after the treatment course (Figure 6) which contains; A: The change in body weight (the difference was 99.86±1.11, 91.33±0.95 and 93.40±0.99 kg for groups I ,II and III respectively), B: The change in the abdomen circumference (the difference was 110.60±1.11, 103.73±1.00 and 101.06±0.98 cm for groups I ,II and III respectively) and C: The change in body mass index (BMI) (the difference was 34.15±0.29, 31.20±0.25and 31.50± 0.26 for groups I ,II and III respectively) during the study. We detect a decrease in the abdomen circumference after the treatment course. Also, body weight decreased so the BMI was improved significantly. Data are in agreement with previous studies which have shown that the olive leaves and apple vinegar modulates the lipid profile [1,2, 23]**.** In general, this study demonstrates that an olive leaves tea and apple cider vinegar rich in polyphenols and flavonoids with lifestyle modification alleviates the cardiometabolic disorders associated with aging. Further studies are required to assess if this treatment is also useful to prevent cardiometabolic alterations in aged humans as well as in experimental models of metabolic syndrome. Likewise, further studies are required to identify which of the specific compounds present in this extract are responsible for the protective cardiometabolic effects.

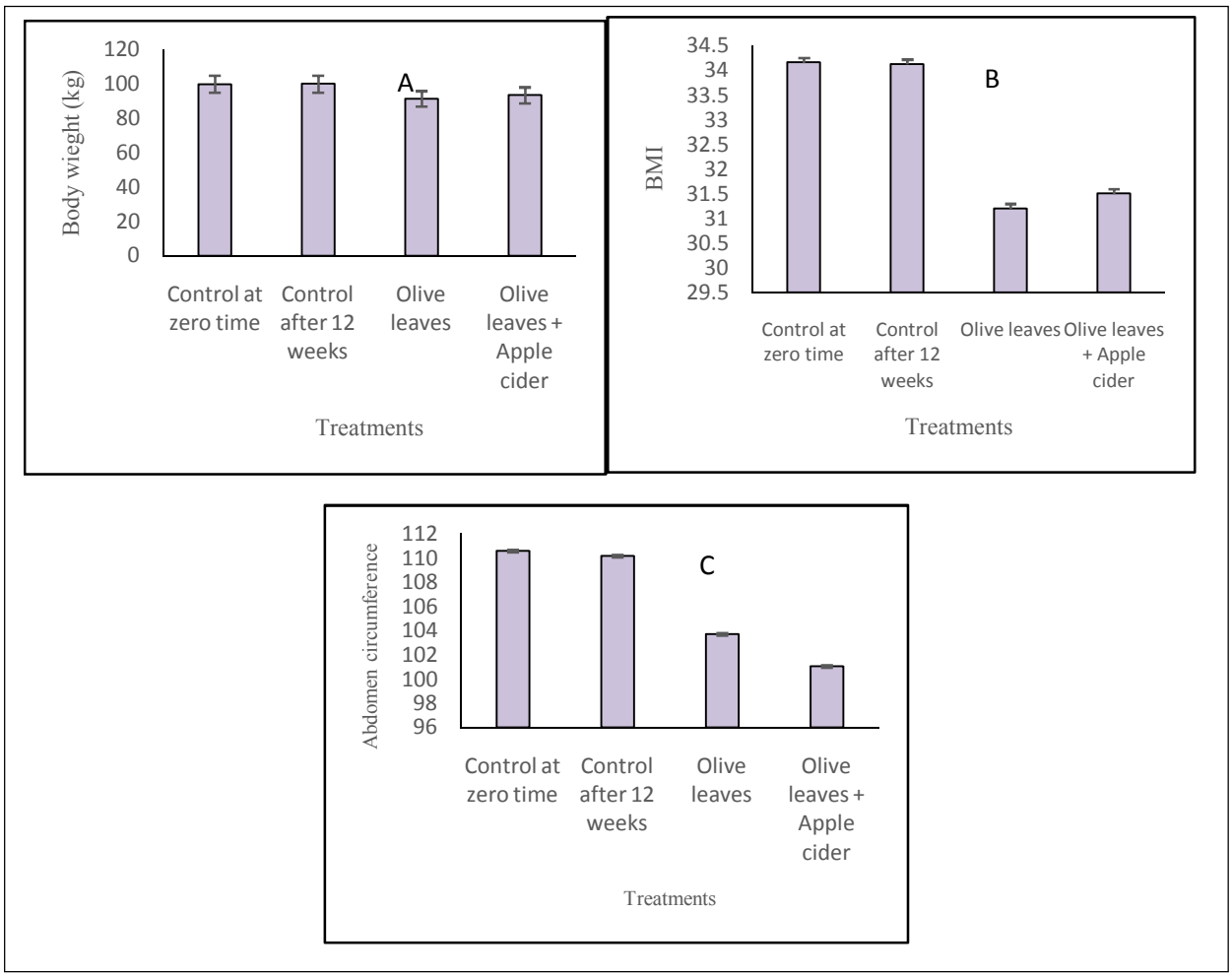

Fig 6: Effect of olive leaves decoction on body measurements

CONCLUSION

Olive leaves tea and apple cider vinegar and their antioxidants (phenolic compounds and flavonoids)have many interesting effects on the human body systems such as, antihypertensive, hypocholesterolemic and hypoglycemic effects. The present study may strengthen the evidences that olive leaves tea and apple cider vinegar have the ability to favorably modify blood pressure, blood glucose and lipid

profiles(metabolic syndrome). The dietary factors and modifying our life style had a good impact in this study towards the primary prevention of hypertension, hyperglycemia and raised cholesterol. In the next few years, there may be clear evidence for this advice to be extended to include foods rich in phenolic compounds. Daily consumption of olive leaves tea and apple cider vinegar can result in lowering blood pressure, blood glucose and serum lipid profiles, and also in favorable improvements in several cardiovascular disease (CVD) risk factors(reducing metabolic syndrome), making it a preferable addition to a healthy diet and lifestyle.

ETHICAL APPROVAL

Ethical approval was granted by the Research Ethical Committee at Faculty of Medicine, Beni-Suef University, (FWA#: FWA00015574). The consent forms were obtained from all group's participants.

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