International Journal of Academic and Applied Research (IJAAR)
ISSN: 2643-9603
Vol. 7 Issue 12, December - 2023, Pages: 181-188

Tea Seed Oil Alleviates Cardiovascular and Hepatic Complications in L-NAME-Induced Hypertensive Rats

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Abstract: *This study investigated the therapeutic potential of Tea (Camellia sinensis) seed oil (TSO) in mitigating hypertension induced by NG-nitro-L-arginine methyl ester (L-NAME) in rats. Forty male Wistar albino rats were divided into five groups, each consisting of eight rats, and subjected to different oral administrations. Group A, designated as the control, received 5 ml/kg of normal saline while groups B-E received 40 mg/kg L-NAME. Additionally, groups C and D received 0.45 and 0.6 ml/kg of TSO, respectively, and group E received the standard drug Enalapril Maleate at 2 mg/kg. These administrations were conducted once daily and extended over a 28-day period. Various parameters, including blood pressure indices, serum lipid profile, serum liver enzyme levels, oxidative stress, and antioxidant enzyme activities in heart and liver tissues, were assessed. The results reveal that TSO administration attenuated L-NAME-induced alterations in blood pressure parameters. TSO also exhibited efficacy in restoring disrupted lipid parameters and reducing elevated liver enzyme activities, demonstrating its potential in ameliorating hyperlipidemia and exerting hepatoprotective effects. Additionally, TSO showed antioxidant properties by decreasing malondialdehyde levels and potentiating the activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and reduced glutathione (GSH) in heart and liver tissues. These findings collectively suggest the therapeutic potential of TSO in alleviating hypertension-related cardiovascular and hepatic complications through its vasodilatory and antioxidant properties.*

Keywords— *Hypertension; Blood Pressure; Tea seed oil; Oxidative stress, Antioxidant*

INTRODUCTION

Hypertension remains the leading risk factor for cardiovascular diseases, and its annihilative effect is felt in the form of reduced life expectancy and premature death. The escalating global incidence of hypertension is linked to factors such as excessive salt intake, physical inactivity, tobacco and alcohol consumption, and the aging process [1]. An individual is considered hypertensive if their systolic blood pressure (SBP) reaches 130 mm Hg or higher and/or if their diastolic blood pressure (DBP) exceeds 80 mm Hg [2].

In developed nations, hypertension ranks as the fourth contributor to premature deaths and seventh in developing countries. Worldwide, nearly 16.5% of annual deaths are attributed to hypertension, and by 2030, this figure is expected to rise to 23.5 million individuals [3, 4]. The prevalence of hypertension in Africa is particularly alarming, with current projections indicating that 150 million people will be affected by 2025, with Nigeria alone accounting for 40 million of this estimate [5].

Throughout history, plants have been explored as an indispensable source of medicine due to their easy affordability and lack of common side effects associated with synthetic drugs [8]. Tea (*Camenlia sinesis*), native to China, stands out as one of the most widely consumed beverages globally. In terms of chemical composition, it encompasses polyphenols, alkaloids, amino acids, polysaccharides, lipids, proteins, vitamins, trace elements, and more [9]. Polyphenols, specifically flavonoids and catechins, constituting approximately 33% of its composition, have been consistently highlighted in various studies as the components that impart the most significant health benefits of tea [10]. Research indicates that tea extract can restore the sperm quality of mice exposed to heat [11], and it has demonstrated relevance in the treatment of dementia due to its dual anti-beta-secretase and anti-cholinesterase activities [12]. Studies, such as [13], have reported the efficacy of tea in inhibiting the proliferation of the colorectal cancer cell line HT-29, as well as its protective role against oxidative damage to DNA.

The present study was aimed at investigating the potential of TSO in mitigating specific clinical complications linked to hypertension in L-NAME-induced hypertensive rats.

MATERIALS AND METHODS

Plant Material and Sample Preparation

Tea seeds were gathered from the Mambilla substation, Cocoa Research Institute of Nigeria (CRIN), Kusuku, Taraba State, Nigeria. The seeds were thoroughly cleaned under running tap water for 3 minutes to eliminate any adhering dirt. Subsequently, the seeds were sun-dried until a consistent weight was achieved, mechanically crushed, and ground to increase the surface area. A 100

g sample of the finely ground tea seeds was introduced into the thimble of a Soxhlet apparatus and then extracted with 500 ml of n-hexane for 6 hours, following the AOCS guidelines [14]. After the extraction, the solvent was eliminated through rotary evaporation at 60^{o}C under a nitrogen stream. The resulting TSO extract was then oven-dried until a stable mass was reached.

Drugs and Chemicals
Enalapril Maleate and NG-nitro-L-arginine methyl ester (L-NAME) were obtained from Honeywell Research Chemicals (Morris Plains, New Jersey). All other chemicals used were obtained from local suppliers and were of analytical grade.

Animals and Experimental Design
A total of forty (40) male Wistar albino rats, with weights ranging from 140 to 200 g, were sourced from the Experimental Animal Unit at the Faculty of Veterinary Medicine, University of Ibadan. These rats were accommodated in adequately ventilated plastic cages and allowed to acclimatize for 14 days prior to the initiation of the experiment. Throughout this acclimatization phase, the rats were provided with commercial rat feed and had unrestricted access to water.

The rats were distributed into five (5) groups of eight rats each. Group A, designated as the control, received 5 ml/kg of normal saline. Groups B-E were subjected to oral administration of 40 mg/kg L-NAME [15] once daily. Furthermore, animals in groups C and D were concurrently administered 0.45 and 0.6 ml/kg of TSO, respectively, while group E received 2mg/kg Enalapril Maleate [16] for a duration of 28 days.

Blood Pressure Measurement
Prior to blood pressure determination, each animal was placed in the holder for 10-15 minutes to ensure proper acclimatization. Blood pressure indices, encompassing systolic (SBP), diastolic (DBP), and mean arterial (MAP) pressures, were non-invasively evaluated using tail plethysmography with an electrosphygnomanometer (CODA, Kent Scientific, USA). A minimum of nine measurements were recorded for each animal, and the mean value was determined.

Blood and Tissue Samples Collection
Following an overnight fasting period, the rats were euthanized using cervical dislocation. Blood was then obtained from each rat via cardiac puncture and collected in sterile plain tubes. The collected blood samples were allowed to clot and subsequently centrifuged at 4000 rpm for 10 minutes. The resulting serum was meticulously separated into another sterile plain tube and stored at 4°C until required. The heart and liver of each rat were then excised, rinsed with a saline solution at a low temperature. The tissues were immersed in liquid nitrogen and promptly preserved at -80°C for subsequent analyses.

Measurement of Lipid Profile
The collected sera were used to assess various lipid components, including total cholesterol (TC), triglycerides (TGs), high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol. The quantification of total cholesterol and triglycerides followed the methods of [17], and [18], respectively. The high-density lipoprotein (HDL) cholesterol level was determined using the method outlined by [19], while the estimation of low-density lipoprotein (LDL) cholesterol employed the Friedewald formula [20]:

$$LDL\text{-}C = (TC) - (HDL\text{-}C) - (TGs/5)$$

Estimation of Liver Function Indices
The activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were assessed following the procedure outlined by [21]. Alkaline phosphatase (ALP) activity was determined using the method described by [22]. Total protein (TP) was quantified using the biuret reaction, as described by [23]. The concentration of albumin (ALB) was determined using the bromocresol green dye-binding method [24]. Serum total and conjugated bilirubins were determined according to the method described by [25] and modified by [26].

Assay of Tissue Oxidative Stress and Antioxidant Enzyme Markers
The heart and liver were individually sectioned into smaller fragments with a sterile scalpel and homogenized in an aqueous solution of 0.1M potassium buffer (pH 7.4). Subsequently, the homogenates underwent centrifugation at 10,000 rpm (4°C) for 10 minutes, and the resulting supernatants were employed for the antioxidant assays. Catalase (CAT) activity was assessed using the method developed by [27]. The activity of superoxide dismutase (SOD) was estimated through the pyrogallol autoxidation method as outlined by [28]. Reduced glutathione (GSH) was determined using the 5,5'-dithiobis-2-nitrobenzoic acid (DTNB) recycling method described by [29]. Glutathione peroxidase (GPx) activity was determined according to the method outlined by [30]. The level of malondialdehyde (MDA) was measured using the method described by [31].

RESULTS

Table 1 depicts the impact of tea seed oil (TSO) on systolic, diastolic, and mean arterial blood pressure in L-NAME-induced hypertensive rats. A statistically significant alteration in systolic blood pressures (SBP) was observed in groups B and E rats compared to the control (A). Similarly, SBP values in groups C, D, and E rats exhibited a significant decrease compared to the hypertensive group B. Administration of TSO at the highest dose (0.6 ml/kg) led to a noteworthy

reduction in diastolic blood pressure (DBP) in group D animals compared to both the control (A) and the hypertensive group (B). A similar result was observed in group E rats administered the standard drug, enalapril maleate. Additionally, it was noted that L-NAME induced a significant increase in mean arterial blood pressure (MAP) in group B rats compared to the control, while group E animals demonstrated a marked reduction in this blood pressure parameter compared to the control (A) and the hypertensive group (B).

Table 1: Effect of tea seed oil on blood pressure parameters

Blood Pressure Parameters (mm Hg)	GroupA (Control)	Group B	Group C	Group D	Group E
SBP	119.57 ± 4.75	124.83 ± 2.63[a]	119.00 ± 13.42[b]	119.42 ± 11.87[b]	108.29 ± 4.03[a,b]
DBP	82.67 ± 6.09	81.00 ± 8.20	80.83 ± 11.75	77.60 ± 9.75[a,b]	73.57 ± 3.10[a,b]
MAP	93.50 ± 3.87	97.75 ± 5.00[a]	93.00 ± 13.68	88.50 ± 11.22	84.86 ± 2.61[a,b]

Values are expressed as mean ± standard deviation (n = 8). A, B, C, D and E represent control, 40 mg/kg L-NAME, 40 mg/kg L-NAME + 0.45 ml/kg TSO, 40 mg/kg L-NAME + 0.6 ml/kg TSO and 40 mg/kg L-NAME + 25m/kg Enalapril Maleate, respectively. [a]P < 0.05 significantly different compared with control (A); [b]P < 0.05 significantly different compared with group B (40 mg/kg L-NAME). SBP- Systolic Blood Pressure; DBP- Diastolic Blood Pressure; MAP- Mean Arterial Blood Pressure.

Table 2: Effect of tea seed oil on serum lipid profile

Parameters (mg/dL)	GroupA (Control)	Group B	Group C	Group D	Group E
TC	158.00 ± 13.64	162.40 ± 13.70	161.60 ± 15.31	152.80 ± 8.64[a,b]	158.20 ± 6.76
TG	58.80 ± 9.47	62.80 ± 8.80	58.80 ± 4.15	79.40 ± 14.27[a,b]	62.80 ± 9.01
HDL-C	42.60 ± 5.94	35.80 ± 6.38	39.84 ± 5.81	49.40 ± 4.22[a,b]	45.80 ± 6.57
LDL-C	132.40 ± 13.94	140.00 ± 17.73[a]	130.00 ± 13.93	122.80 ± 12.54[a,b]	129.80 ± 13.04

Values are expressed as mean ± standard deviation (n = 8). A, B, C, D and E represent control, 40 mg/kg L-NAME, 40 mg/kg L-NAME + 0.45 ml/kg TSO, 40 mg/kg L-NAME + 0.6 ml/kg TSO and 40 mg/kg L-NAME + 25m/kg Enalapril Maleate, respectively. [a]P < 0.05 significantly different compared with control (A); [b]P < 0.05 significantly different compared with group B (40 mg/kg L-NAME). TC- Total Cholesterol; TG- Triglyceride; HDL-C- High-Density Lipoprotein Cholesterol; LDL-C- Low-Density Lipoprotein Cholesterol.

observed for alanine aminotransferase (ALT) and alkaline phosphatase (ALP). The total protein (TP) value in group B significantly decreased compared to the control, while group E exhibited a significant decrease in the albumin (ALB)

Table 2 shows the impact of tea seed oil on the serum lipid profile in rats with L-NAME-induced hypertension. Group D rats exhibited a significant alteration in the values of all measured lipid parameters compared to both the control and hypertensive group B. Additionally, group B rats, subjected only to L-NAME administration, exhibited a notable increase in LDL-C compared to the control (A).

Table 3 illustrates the impact of tea seed oil on serum liver enzyme activities in L-NAME-induced hypertensive rats. There was a notable increase in the aspartate aminotransferase (AST) value in group B compared to the control. However, the administration of tea seed oil (TSO) at various doses resulted in a significant decrease in AST values in groups C and D compared to group B animals. In group E, there was also a significant reduction in the AST value compared to group B animals. Similar results were

value compared to the control. Additionally, in group E, total bilirubin (TB) decreased significantly compared to both the control and group B.

Table 4 illustrates the effect of tea seed oil on malondialdehyde level and antioxidant enzyme activities in heart tissue homogenate of L-NAME-induced hypertensive rats. Malondialdehyde (MDA) levels in group B exhibited a significant increase compared to the control (Group A). Catalase decreased significantly in groups B and C compared to the control (A) but showed a significant increase in group C compared to group B. The value of superoxide dismutase (SOD) in group B significantly decreased compared to the control but significantly increased in groups C, D, and E compared to group B. The results obtained for glutathione

peroxidase (GPx) and glutathione (GSH) were also akin to those observed for SOD.

Table 3: Effect of tea seed oil serum liver enzyme activities

Parameters	GroupA (Control)	Group B	Group C	Group D	Group E
AST (U/L)	156.20 ± 1.30	259.20 ± 2.59[a]	168.20 ± 1.79[b]	165.00 ± 1.58[b]	161.40 ± 1.14[b]
ALT (U/L)	88.60 ± 1.14	184.60 ± 1.95[a]	80.60 ± 2.07[b]	82.31 ± 1.82[b]	78.20 ± 0.84[b]
ALP (U/L)	175.20 ± 5.89	266.52 ± 6.89[a]	184.00 ± 7.07[b]	182.00 ± 10.61[b]	165.60 ± 7.57[a,b]
TP (g/dL)	7.14 ± 0.13	6.70 ± 0.21[a]	7.10 ± 0.19	7.10 ± 0.21	7.58 ± 0.16
ALB (g/dL)	4.02 ± 0.15	3.62 ± 0.24	3.98 ± 0.23	3.96 ± 0.25	4.52 ± 1.23[b]
TB (mg/dL)	0.52 ± 0.16	0.56 ± 0.15	0.54 ± 0.26	0.70 ± 0.21[a,b]	0.52 ± 0.13
CB (mg/dL)	0.30 ± 0.07	0.30 ± 0.10	0.26 ± 0.11	0.34 ± 0.17	0.25 ± 0.09

Values are expressed as mean ± standard deviation (n = 8). A, B, C, D and E represent control, 40 mg/kg L-NAME, 40 mg/kg L-NAME + 0.45 ml/kg TSO, 40 mg/kg L-NAME + 0.6 ml/kg TSO and 40 mg/kg L-NAME + 25m/kg Enalapril Maleate, respectively. [a]$P < 0.05$ significantly different compared with control (A); [b]$P < 0.05$ significantly different compared with group B (40 mg/kg L-NAME). AST- Aspartate aminotransferase; ALT- Alanine aminotransferase; ALP- Alkaline Phosphatase; TP- Total Protein; ALB- Albumin; TB- Total Bilirubin; CB- Conjugated Bilirubin

catalase values in groups C, D, or E compared to either group A or B. In comparison with the control, group B exhibited a significant decrease in the content of SOD. Conversely, in groups C, D, and E, the values of SOD were significantly increased compared to group B. Groups B and C displayed a significant decrease in the value of glutathione peroxidase (GPx) compared to the control (A), while Group C exhibited a significantly higher quantity of GPx compared to group B. Groups D and E showed no significant difference in GPx values compared to either the control (Group A) or group B. The values of reduced glutathione (GSH) were significantly elevated in the two TSO-treated groups (Groups C and D) and the group administered the standard drug, compared to either the control (Group A) or group B.

Table 5 shows the impact of tea seed oil on malonaldehyde level and antioxidant enzyme activities in liver tissue homogenate of L-NAME-induced hypertensive rats. The malondialdehyde (MDA) value in group B rats significantly increased compared to the control (Group A). Although not statistically significant, the administration of TSO in groups C and D reduced the MDA content closer to that of the control (Group A). In group E, the MDA value changed significantly compared to both the control and group B. A noticeable decrease was observed in the measured value of catalase (CAT) in group B compared to the control (Group A). However, no significant alterations were noted in the

DISCUSSION

Apart from its widespread popularity as a beverage, different varieties of tea have been linked to a spectrum of medicinal properties. The health-promoting effects are frequently ascribed to the existence of bioactive compounds, encompassing polyphenols, catechins, and antioxidants [32]. The chronic application of NG-nitro-L-arginine methyl ester (L-NAME) represents a model for the development of experimental hypertension [33]. L-NAME is a competitive inhibitor of nitric oxide synthase (NOS), the enzyme responsible for the synthesis of nitric oxide from L-arginine [34]. In this study, L-NAME is utilized to induce hypertension, allowing for the exploration of the potential therapeutic properties elucidated by TSO in rat models.

Blood Pressure Parameters

The concurrent administration of TSO at varying doses with L-NAME in groups C and D mitigated the hypertensive effects observed in group B. The reversal of the blood pressure parameters may have occurred as a result of the vasodilatory effect of TSO, as corroborated in a study

conducted by [35], where healthy subjects were included in a

double-blind, placebo-controlled, randomized, crossover

Table 4: Effect of tea seed oil on malonaldehyde and antioxidant enzyme activities in heart tissue homogenate of rats

Table 5: Effect of tea seed oil on malonaldehyde level and antioxidant enzyme activities in liver tissue homogenate of rats

Parameters	GroupA (Control)	Group B	Group C	Group D	Group E
MDA (nmol/mg protein)	13.31 ± 5.13	26.11 ± 2.30[a]	12.32 ± 5.21	12.62 ± 4.81	11.23 ± 1.37
CAT (U/mg protein)	10.13 ± 0.71	22.61 ± 4.43[a]	13.32 ± 2.26	14.45 ± 5.11	12.21 ± 6.39[a,b]
SOD (U/mg protein)	60.18 ± 7.24	38.57 ± 8.25[a]	49.80 ± 4.15[a,b]	59.38 ± 38.16	64.12 ± 2.83
GPx (U/mg protein)	60.31 ± 5.11	30.42 ± 3.37[a]	55.38 ± 6.28	58.82 ± 8.32	67.12 ± 4.53
GSH (µmol/g protein)	10.27 ± 2.62	4.42 ± 5.70[a]	12.89 ± 0.94[b]	10.26 ± 16.35[b]	14.00 ± 1.24[b]
	13.72 ± 0.73	8.42 ± 1.14[a]	10.62 ± 2.47[b]	15.18 ± 3.42[b]	12.00 ± 2.71[b]
	20.31 ± 2.75	10.21 ± 8.02[a]	18.16 ± 2.82[b]	20.14 ± 13.36[b]	22.46 ± 3.63[b]
	16.48 ± 7.01	9.43 ± 6.38[a]	12.00 ± 6.75[a,b]	17.19 ± 2.76	19.56 ± 7.38
	7.71 ± 2.92	3.28 ± 4.39[a]	6.87 ± 1.46[b]	7.37 ± 1.29[b]	7.11 ± 3.16[b]
	5.84 ± 9.20	5.14 ± 0.12	8.50 ± 5.11[a,b]	8.87 ± 7.45[a,b]	7.85 ± 0.67[a,b]

Values are expressed as mean ± standard deviation (n = 8). A, B, C, D and E represent control, 40 mg/kg L-NAME, 40 mg/kg L-NAME + 0.45 ml/kg TSO, 40 mg/kg L-NAME + 0.6 ml/kg TSO and 40 mg/kg L-NAME + 25m/kg Enalapril Maleate, respectively. [a]P < 0.05 significantly different compared with control (A); [b]P < 0.05 significantly differencompared with group B (40 mg/kg L-NAME). MDA- Malondialdehyde; CAT- Catalase; SOD- Superoxide Dismutase; GSH- Reduced Glutathione; GPx- Glutathione peroxidase.

study. Subjects received capsules with a single dose of catechins (500 mg), four varying doses of theaflavins (100 to 500 mg), or placebo. Microcirculation was assessed and found to improve after each treatment.

Serum Lipid Profile

Hypertension is closely intertwined with lipid metabolism, and frequently, irregularities in lipid profile coexist with this cardiovascular condition. Hypertension is often linked to an increase in total cholesterol levels, which includes LDL-C, HDL-C, and a fraction of triglycerides [36]. Elevated levels of LDL-C contributes to the accumulation of plaques within arterial walls, resulting in atherosclerosis and compromising the flow of blood while high-density lipoprotein cholesterol (HDL-C) exhibits a protective role by transporting cholesterol away from arteries to the liver for excretion. In individuals with hypertension, there could be a reduction in HDL-C levels, diminishing this protective effect and exacerbating the atherosclerotic process [37, 38]. Triglycerides, a form of fat in the bloodstream, can also contribute to the onset of atherosclerosis when their levels are elevated [39]. The present study also demonstrated that the administration of L-NAME resulted in changes in the lipid profile of the animals, especially in group D rats. These alterations were subsequently restored to values closely resembling those of the control group (A) through the concurrent administration of TSO. Various studies have demonstrated the efficacy of tea consumption in reducing hyperlipidemia. For example, in a randomized, placebo-controlled clinical trial conducted by [40], subjects treated with four capsules of green tea extracts, totaling 1315 mg of catechins per day for 12 months, experienced a significant decrease in blood total cholesterol (TC) and LDL-cholesterol (LDL-C) levels. This reduction was particularly notable in individuals with elevated baseline TC levels.

Serum Liver Enzyme Activities

The growing awareness of the interconnection betwbetween the onset of hypertension and liver dysfunction is evident. The liver enzymes alanine and aspartate aminotransferase (ALT and AST), γ-glutamyltransferase (GGT), and alkaline phosphatase (ALP) are commonly employed as reliable indicators of liver health [41]. Elevated levels of these enzymes in the bloodstream are linked to heightened levels of inflammatory markers. This can lead to systemic inflammation and oxidative stress, potentially affecting endothelial function and playing a role in the development of hypertension [42]. The observed increase in liver enzymes (AST, ALT, ALP) in group B suggests that L-NAME may directly or indirectly contribute to hepatic stress. The concurrent administration of TSO in groups C and D seems to confer hepatoprotective effects through its antioxidant properties, which counteract the oxidative stress induced by L-NAME. This could elucidate the notable decrease in AST levels observed in these groups compared to

group B. The decrease in total protein (TP) in group B suggests a disruption in protein metabolism induced by L-NAME. This could be related to decreased synthesis or increased breakdown of proteins in the liver [43]. The significant decrease in albumin (ALB) levels in group E raises questions about the specific influence of Enalapril Maleate on albumin synthesis or metabolism.

Malonaldehyde Level and Antioxidant Enzyme Activities in Heart Tissue Homogenate of Rats

Malondialdehyde (MDA) is a marker of lipid peroxidation, and the significant increase in group B suggests that L-NAME administration induces oxidative stress in the heart. This aligns with the known role of L-NAME in impairing nitric oxide (NO) synthesis. NO is known for its antioxidant properties, and its depletion may contribute to increased oxidative stress [44]. Elevated oxidative stress results in lipid peroxidation, leading to the observed rise in MDA levels in group B. Catalase, an important antioxidant enzyme involved in breaking down hydrogen peroxide (H_2O_2) into water and oxygen [45], showed a significant decrease in groups B and C. This indicates a potential reduction in the ability to neutralize reactive oxygen species (ROS). However, the increase in group C suggests a therapeutic impact and/or compensatory response of TSO. Superoxide dismutase (SOD) is responsible for neutralizing superoxide radicals [46]. The initial decrease in group B suggests a compromised antioxidant defense and the subsequent increase in groups C, D, and E implies that TSO may enhance SOD activity, possibly by reducing the superoxide ($O_2^{\bullet-}$) burden or promoting SOD synthesis. Glutathione peroxidase (GPx) and reduced glutathione (GSH) are integral components of the cellular antioxidant defense system that function to eliminate reactive oxygen species (ROS) and reactive nitrogen species (RNS) [47]. The parallel changes observed in these enzymes mirror SOD dynamics, indicating a restorative response to oxidative stress by TSO through the potentiation of these antioxidant mechanisms.

Malonaldehyde Level and Antioxidant Enzyme Activities in Liver Tissue Homogenate of Rats

As earlier mentioned, the observed elevation in MDA levels in the group treated solely with L-NAME indicates increased lipid peroxidation, consistent with reduced NO availability. The decrease in CAT, SOD, and GPx levels in this group further support the induction of oxidative stress in this model. The observed changes in oxidative stress markers and antioxidant enzymes in the TSO-treated groups (C and D) collectively indicate an attempt by the system to restore redox balance. TSO may contribute to this homeostasis by reducing ROS production, enhancing antioxidant defenses, and modulating cellular redox signaling pathways [48].

Values are expressed as mean ± standard deviation (n = 8). A, B, C, D and E represent control, 40 mg/kg L-NAME, 40 mg/kg L-NAME + 0.45 ml/kg TSO, 40 mg/kg L-NAME + 0.6 ml/kg TSO and 40 mg/kg L-NAME + 25m/kg Enalapril Maleate, respectively. $^{a}P < 0.05$ significantly different compared with control (A); $^{b}P < 0.05$ significantly differencompared with group B (40 mg/kg L-NAME). MDA- Malondialdehyde; CAT- Catalase; SOD- Superoxide Dismutase; GSH- Reduced Glutathione; GPx- Glutathione peroxidase

CONCLUSION

This study affirms the therapeutic potential of TSO in addressing complications associated with hypertension, particularly in cardiovascular and hepatic contexts. While further research is warranted to elucidate the underlying mechanisms, the present study provides valuable insights into the multifaceted benefits of TSO, positioning it as a natural and potentially effective agent in the management of hypertension and its associated complications.

CONFLICTS OF INTEREST

None declared.

REFERENCES

[1] Wang, J. G., Zhang, W., Li, Y., & Liu, L. (2023). Hypertension in China: epidemiology and treatment initiatives. *Nature Reviews Cardiology*, 1-15.

[2] Muntner, P., Shimbo, D., Carey, R. M., Charleston, J. B., Gaillard, T., Misra, S., & Wright Jr, J. T. (2019). Measurement of blood pressure in humans: a scientific statement from the American Heart Association. *Hypertension*, *73*(5), 35-66.

[3] Kibret, K. T., & Mesfin, Y. M. (2015). Prevalence of hypertension in Ethiopia: a systematic meta-analysis. *Public health reviews*, *36*(1), 1-12.

[4] Oliveira, G. M. M. D., Brant, L. C. C., Polanczyk, C. A., Malta, D. C., Biolo, A., Nascimento, B. R., & Ribeiro, A. L. P. (2022). Cardiovascular Statistics–Brazil 2021. *Arquivos Brasileiros de Cardiologia*, *118*, 115-373.

[5] Akindele, M. O. (2014). An intervention programme for management of overweight and obese Nigerians in Lagos State, Nigeria.

[6] Zhao, Y., Vanhoutte, P. M., & Leung, S. W. (2015). Vascular nitric oxide: Beyond eNOS. *Journal of pharmacological sciences*, *129*(2), 83-94.

[7] Kanthlal, S. K., Joseph, J., Paul, B., & P, U. D. (2020). Antioxidant and vasorelaxant effects of aqueous extract of large cardamom in L-NAME induced hypertensive rats. *Clinical and experimental hypertension*, *42*(7), 581-589.

[8] Parasuraman, S. (2018). Herbal drug discovery: challenges and perspectives. *Current Pharmacogenomics and Personalized Medicine (Formerly Current Pharmacogenomics)*, *16*(1), 63-68.

[9] Suna, S., Tamer, C. E., & Özcan-Sinir, G. (2019). Trends and possibilities of the usage of medicinal herbal extracts in beverage production. In *Natural beverages* (pp. 361-398). Academic Press.

[10] Vishnoi, H., Bodla, R. B., Kant, R., & Bodla, R. B. (2018). Green tea (Camellia sinensis) and its antioxidant property: a review. *International Journal of Pharmaceutical Sciences and Research*, *9*(5), 1723-36.

[11] Mahmoudi, R., Azizi, A., Abedini, S., Jahromi, V. H., Abidi, H., & Barmak, M. J. (2018). Green tea improves rat sperm quality and reduced cadmium chloride damage effect in spermatogenesis cycle. *Journal of medicine and life*, *11*(4), 371.

[12] Suttisansanee, U., Kunkeaw, T.,Tthatsanasuwan, N., Tonglim, J., & Temviriyanukul, P. (2019). The Investigation on Cholinesterases and BACE1 Inhibitory Activities in Various Tea Infusions. *Walailak Journal of Science and Technology (WJST)*, *16*(3), 165-174.

[13] Wang, S. T., Cui, W. Q., Pan, D., Jiang, M., Chang, B., & Sang, L. X. (2020). Tea polyphenols and their chemopreventive and therapeutic effects on colorectal cancer. *World journal of gastroenterology*, *26*(6), 562.

[14] Irving, G.W. (1958). A.O.C.S. commentary: Guidelines for research on fats and oils in the United States Department of Agriculture. *Journal of the American Oil Chemists' Society*, *35*(4).

[15] Metchi Donfack, M. F., Atsamo, A. D., Temdié Guemmogne, R. J., Ngouateu Kenfack, O. B., Dongmo, A. B., & Dimo, T. (2021). Antihypertensive effects of the Vitex cienkowskii (Verbenaceae) stem-bark extract on L-NAME-induced hypertensive rats. *Evidence-based Complementary and Alternative Medicine*, *2021*, 1-10.

[16] Tawfeek, H. M., Faisal, W., & Soliman, G. M. (2018). Enalapril maleate orally disintegrating tablets: tableting and in vivo evaluation in hypertensive rats. *Pharmaceutical Development and Technology*, *23*(5), 496-503.

[17] Roeschlau, P., Bernt, E., & Gruber, W. (1974). Enzymatic determination of total cholesterol in serum. *Zeitschrift für Klinische Chemie und Klinische Biochemie*, *12*, 226–7.

[18] Biggs, H. G., Erikson, J. M., & Moorehead, W. R. (1975). A manual colorimetric assay of triglycerides in serum. *Clinical Chemistry*, *21*(3), 437-441.

[19] Warnick, G. R., Nauck, M., & Rifai, N. (2001). Evolution of methods for measurement of HDL-cholesterol: From ultracentrifugation to homogeneous assays. *Clinical Chemistry*, *47*(9), 1579-1596.

[20] Krishnaveni, P., & Gowda, V. M. (2015). Assessing the validity of Friedewald's formula and Anandraja's formula for serum LDL-cholesterol calculation. *Journal of clinical and diagnostic research: JCDR*, *9*(12), BC01.

[21] Reitman, S., & Frankel, S. (1957). A colorimetric determination of serum glutamic oxalo-acetic and glutamic pyruvic transaminase. *American Journal of Clinical Pathology*, *28*(16), 59–63.

[22] Babson, A. L., Greeley, S. J., Coleman, C. M., & Philips, G. D. (1966). Phenolphthalein mono-phosphate as a substrate for serum alkaline phosphatase. *Clinical Chemistry*, *12*, 482-490.

[23] Linne, J. J., & Ringsurd, K. K. (1979). *Basic Technique for the Medical Laboratory* (Ed.). McGraw-Hall Book Company, New York.

[24] Doumas, B. T., Watson, W. A., & Biggs, H. G. (1971). Albumin standards and the measurement of serum albumin with bromcresol green. *Clinica Chimica Acta*, *31*(1), 87-96.

[25] Malloy, H. T., & Evelyn, K. A. (1937). Measurement of plasma bilirubin (modified). *Journal of Biological Chemistry*, *119*(2), 481.

[26] Nwanjo, H. U., & Alumanah, E. O. (2006). Effect of aqueous extract of Gongronema latifolium on some indices of liver function in rats. *Global Journal of Medical Sciences*, *5*(1), 17-20.

[27] Goth, L. (1991). A simple method for determination of serum catalase activity and revision of reference range. *Clinical Chimica Acta*, *196*, 143-151.

[28] Marklund, S., & Marklund, G. (1974). Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase. *European Journal of Biochemistry*, *47*, 469–474.

[29] Banerjee, B., Seth, V., Bhattacharya, A., Pasha, S., & Chakraborty, A. (1999). Biochemical effects of some pesticides on lipid peroxidation and free-radical scavengers. *Toxicology Letters*, *107*(1), 33-47.

[30] Kinoshita, C., Saze, K. I., Kumata, S., Matsuki, T., & Homma, S. (1996). A simplified method for the

estimation of glutathione peroxidase activity and selenium concentration in bovine blood. *Journal of Dairy Science*, *79*(9), 1543–1548.

[31] Okhawa, H., Ohishi, N., & Yagi, K. (1979). Assay for lipid peroxides in animal tissues by thiobarbituric acid. *Analytical Biochemistry*, *95*, 351-358.

[32] Musial, C., Kuban-Jankowska, A., & Gorska-Ponikowska, M. (2020). Beneficial properties of green tea catechins. *International journal of molecular sciences*, *21*(5), 1744.

[33] Adedapo, A. D., Ajayi, A. M., Ekwunife, N. L., Falayi, O. O., Oyagbemi, A., Omobowale, T. O., & Adedapo, A. A. (2020). Antihypertensive effect of Phragmanthera incana (Schum) Balle on NG-nitro-L-Arginine methyl ester (L-NAME) induced hypertensive rats. *Journal of ethnopharmacology*, *257*, 112888.

[34] Krasylenko, Y. A., Yemets, A. I., & Blume, Y. B. (2019). Nitric oxide synthase inhibitor L-NAME affects Arabidopsis root growth, morphology, and microtubule organization. *Cell Biology International*, *43*(9), 1049-1055.

[35] Fuchs, D., De Graaf, Y., Van Kerckhoven, R., & Draijer, R. (2014). Effect of tea theaflavins and catechins on microvascular function. *Nutrients*, *6*(12), 5772-5785.

[36] Lee, Y., & Siddiqui, W. J. (2019). Cholesterol levels.

[37] Khatana, C., Saini, N. K., Chakrabarti, S., Saini, V., Sharma, A., Saini, R. V., & Saini, A. K. (2020). Mechanistic insights into the oxidized low-density lipoprotein-induced atherosclerosis. *Oxidative medicine and cellular longevity*, *2020*.

[38] Ben-Aicha, S., Badimon, L., & Vilahur, G. (2020). Advances in HDL: much more than lipid transporters. *International Journal of Molecular Sciences*, *21*(3), 732.

[39] Packard, C. J., Boren, J., & Taskinen, M. R. (2020). Causes and consequences of hypertriglyceridemia. *Frontiers in endocrinology*, *11*, 252.

[40] Samavat, H., Newman, A. R., Wang, R., Yuan, J. M., Wu, A. H., & Kurzer, M. S. (2016). Effects of green tea catechin extract on serum lipids in postmenopausal women: a randomized, placebo-controlled clinical trial. *The American journal of clinical nutrition*, *104*(6), 1671-1682.

[41] Rahman, S., Islam, S., Haque, T., Kathak, R. R., & Ali, N. (2020). Association between serum liver enzymes and hypertension: a cross-sectional study in Bangladeshi adults. *BMC cardiovascular disorders*, *20*, 1-7.

[42] Strnad, P., Tacke, F., Koch, A., & Trautwein, C. (2017). Liver-guardian, modifier and target of sepsis. *Nature reviews Gastroenterology & hepatology*, *14*(1), 55-66.

[43] Yang, C. S., Zhang, J., Zhang, L., Huang, J., & Wang, Y. (2016). Mechanisms of body weight reduction and metabolic syndrome alleviation by tea. *Molecular nutrition & food research*, *60*(1), 160-174.

[44] Tan, B. L., Norhaizan, M. E., Liew, W. P. P., & Sulaiman Rahman, H. (2018). Antioxidant and oxidative stress: a mutual interplay in age-related diseases. *Frontiers in pharmacology*, *9*, 1162.

[45] Zulaikhah, S. T. (2017). The role of antioxidant to prevent free radicals in the body. *Sains Medika Journal of Medical & Health*, *8*(1).

[46] Maurya, R., & Namdeo, M. (2021). Superoxide dismutase: a key enzyme for the survival of intracellular pathogens in host. *Reactive Oxygen Species*.

[47] Panday, S., Talreja, R., & Kavdia, M. (2020). The role of glutathione and glutathione peroxidase in regulating cellular level of reactive oxygen and nitrogen species. *Microvascular Research*, *131*,

[48] Yan, Z., Zhong, Y., Duan, Y., Chen, Q., & Li, F. (2020). Antioxidant mechanism of tea polyphenols and its impact on health benefits. *Animal Nutrition*, *6*(2), 115-123.