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Original Article

Effectiveness of Mango Mistletoe on Lung Superoxide Dismutase in Hypertensive Rats Exposed to DOCA-Salt

Surya Darma[1], Evelyn Angie[1*], Yuliani Mardiati Lubis[1], Firdha Muharraran[1]

[1] Department of Biomedicine, University of Prima Indonesia, Medan, Indonesia

(Correspondence author's email, evelyn.angie97@gmail.com)

ABSTRACT

Vascular disease, caused by oxidative stress and endothelial cell inflammation during hypertension's development, produces substantial mortality and morbidity. Mango mistletoe was tested for its effect on pulmonary superoxide dismutase (SOD) in hypertensive rats exposed to DOCA-salt in a preventative model. This study involves experimental quantitative research. SPSS was used for one-way ANOVA and post-hoc LSD testing. The population used was male Wistar rats (Rattus norvegicus). The samples used were 25 male Wistar rats divided into five treatment groups because of the Shapiro-Wilk test for normality analysis. The treatment group included a negative control group, a positive control group, and a group given different doses of mango mistletoe methanol extract: P1 at 75 mg/kgBW, P2 and P3 at 150 mg/kgBW, and P3 at 250 mg/kgBW. The study indicated that 250 mg/kg BW mango mistletoe extract increased SOD levels in DOCA-Garam-exposed Wistar white rats (Rattus norvegicus). Enhanced superoxide dismutase, malondialdehyde (MDA), ureum, creatinine, and renal histology see this. The normality of study data in the complete group assessing SOD, MDA, ureum, and creatinine levels showed a significance value larger than 0.05. The significance probability and one-way ANOVA test values are more than 0.05. The study found that mango mistletoe extract contains saponins, tannins, flavonoids, and triterpenoids that increase SOD levels and repair kidney cells damaged by hypertension in Wistar white rats. The study examined how mango mistletoe extract affects mouse hypertension. However, its conclusions should not be applied to humans. Clinical trials are needed to determine mango mistletoe extract's safety and efficacy for humans.

Keywords: *Mango Mistletoe, Superoxide Dismutase, Malondialdehyde, Ureum, Creatinine*

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INTRODUCTION

Humans have used plant-derived medications for thousands of years [1]. Many around the globe rely on plant-based medicine due to its accessibility and lack of other healthcare options. Many countries, including China, Indonesia, and most African nations, use plant-based or herbal medications to treat various disorders [2]. Many countries treat multiple diseases with plant extracts, mixtures, poultices, decoctions, or pastes. Since antiquity, several medicinal plants and plant-based techniques have been known for their therapeutic effects on healing [3].

The oxidative stress and inflammation of endothelial cells that occur throughout the development of hypertension contribute to the high mortality and morbidity associated with vascular disease, which is one of the causes of hypertension [4]. Hypertension and other cardiovascular disease problems are greatly amplified in response to oxidative stress [5-7]. Hence, it can alleviate hypertension by reducing inflammation and oxidative stress in endothelial

cells. Genetic and environmental variables combine in intricate ways to cause hypertension, a multifactorial disease in and of itself. Hypertension can be caused or worsened by reactive oxygen species (ROS) that are present in excess. Artery occlusion (atherosclerosis) is caused by LDL oxidation. Untreated oxidized LDL has the potential to cause hypertension [8-10].

Oxidative stress happens when reactive oxygen species (ROS) rise above what the body's natural defenses can handle. High amounts of malondialdehyde and reduced superoxide dismutase activity are indicators of oxidative stress caused by excess lipid peroxidation in cells. Intracellular antioxidant enzymes are the body's natural defense against reactive oxygen species (ROS) processing [11]. Enzymes like catalase, glutathione peroxidase, and superoxide dismutase are found inside cells and work to neutralize free radicals [12]. These three enzymes have distinct distributions in various bodily tissues and organs, including the liver, kidneys, heart, and spleen [13].

Scavenging superoxide anions produced in the early phases of oxidative stress and delaying aging are significant functions of superoxide dismutase (SOD) [12]. Superoxide anions can be converted into oxygen and hydrogen peroxide, two more stable molecules, using antioxidant initiators [12,14]. An external source of oxygen is required to compensate for the absence of antioxidants within cells and to neutralize the resulting radicals [15].

Huang et al. (2018) found that several elements impact the physiological system that controls blood pressure and involve intricate interactions between environmental and genetic components [16]. A condition known as hypertension or high blood pressure occurs when either the systolic or diastolic blood pressure is equal to or greater than 140 mmHg or 90 mmHg, respectively. Many people refer to hypertension as "the silent killer" because the condition rarely causes any noticeable symptoms; as a result, many people with hypertension are unaware that they have it until they develop a problem from it. Healthcare providers diagnose hypertension in just 36.8% of patients, and treatment adherence is low at only 0.7% [17].

Despite being a semi-parasitic plant, the bioactivities of mango mistletoe may be host plant-dependent [18]. According to research reports, mango mistletoe may have many medical uses, including as an antioxidant [19], anti-inflammatory [20], cytotoxic [19-21], hepatoprotective [22], immunomodulatory [23], anti-aging agent [24], and against cancer [25], anti-bacterial [26], anti-cancer [25], hyperglycemia, and proliferative diseases. According to phytochemical research, mango mistletoe contains alkaloids, phenolics, flavonoids, saponins, and terpenoids [27].

Manganese mistletoe (*Dendrophthoe pentandra*) has several uses in human medicine, including the treatment of hypertension, according to several scientific research [18-19]. The parasite of the mango plant, often known as mango mistletoe, has been shown in studies to have antihypertensive and anticancer properties [19-20]. Results from studies evaluating the safety and toxicity of mango mistletoe as a phytopharmaceutical preparation in female Wistar rats have shown that it is not hazardous to their kidneys or lipid profiles [21-22]

Previous work by Aini et al. (2021) utilizing a curative model demonstrated that a methanol extract from mango mistletoe can enhance lung SOD levels in rats with DOCA-Salt-induced hypertension [32]. Mango mistletoe methanol extract is an antioxidant that can relieve oxidative stress by increasing superoxide dismutase (SOD) and lowering malondialdehyde (MDA). To find out if mistletoe manga extract affected serum SOD activity in a preventative model of hypertension in rats induced by DOCA-Garam, this study took a different tack. To avoid hypertension, the preventive model is implemented.

Several phytochemical components have been isolated from mango mistletoe by employing extraction methods like maceration and reflux. This research aims to fill gaps in our knowledge of the phytomorphology, phytochemistry, and extraction methods of mango mistletoe in animals with hypertension and to explore its potential future uses.

METHOD

Laboratory research utilizing a genuine experiment or experimental design is what this study employs as its method of experimental quantitative research [34]. This study used 25 male Wistar rats (Rattus norvegicus). Two months old, 150-200 grams, healthy, and without anatomical anomalies, divided into five groups of five animals and treated for 28 days. The control group (male white rats) received no

treatment. They receive basic food and water. Experimental mice are induced to become hypertensive by administering 1.5 ml/kg prednisone and 25% NaCl for 14 days. Mango mistletoe extract was skipped for 28 days. The mice in Group 1 (P1) were provided standard food and water during adaption. After adaption, this group received mango mistletoe extract 75 mg/kg BW/rat/day for 28 days. The mice in Group 2 (P2) were provided standard food and water during adaption. After adaption, this group received 150 mg/kg BW/rat/day mango mistletoe extract for 28 days. The mice in Group 3 (P3) were provided standard food and water during adaption. After adaption, this group received mango mistletoe extract 250 mg/kg BW/rat/day for 28 days.

Male Wistar rats (Rattus norvegicus) weighing 160-200 grams and 2-3 months old were used in this sample study. Male Wistar rats, one of the most often used biomedical research species, were chosen as test subjects because they have traits and physiologies similar to humans. Inclusion and exclusion criteria determined the sample. Male Wistar rats (Rattus norvegicus), two months old, 150-200 grams, healthy, not physically malformed, and hypertensive are included. Excluded mice did not develop sickness during adaption or perish during treatment.

The one-way ANOVA test was used for data analysis, and the Post Hoc LSD test was used for follow-up testing. ANOVA (Analysis of variances) is the tool for comparing variables across several variables. Only with two variables can the "t" test, a method of comparative analysis that involves comparing two means, be practical. When looking for statistically significant differences between groups, the LSD Post Hoc Test is an excellent tool to use. An asterisk (*) indicates that all groups in this study had significant differences from other groups according to the results of the Post Hoc LSD test analysis[35]. After applying the Kolmogorov-Smirnov test to the data, we found it normally distributed ($p > 0.05$). A one-way analysis of variance technique, also known as One-way ANOVA, was used to examine the significance between groups at a 95% confidence level ($p < 0.05$). Using the Post Hoc Test with the LSD procedure, additional analysis or testing was conducted. If the ANOVA test finds significant differences (Ho is rejected), multiple comparison analysis (Post Hoc Test) attempts to determine further which groups have different averages.

October 2023 to December 2023 is the start of the research period. The research sites were the University of North Sumatra's Anatomical Pathology Laboratory and the Department of Pharmaceutical Pharmacology's Laboratory.

Research procedures carried out mango mistletoe extract (Dendrophthoe pentandra), phytochemical screening, examination of lung SOD levels, assessment of MDA levels, kidney histopathological examination, and administration of treatment doses to experimental subjects. Next, the data results were analyzed using SPSS.

This study examined the Independent Variable (Mango Mistletoe Extract) and the Dependent Variable (SOD, MDA, Ureum, and Creatinine levels in doc-salt-exposed hypertensive rats). Mango mistletoe was macerated and administered at 75 mg/kgBW, 150 mg/kgBW, and 250mg/kgBW for 28 days in the significant variable.

Blood pressure was measured without anesthesia using the tail-cuff auto-pickup method on experimental animals. A CODA® non-invasive blood pressure monitor was used twice a week. A tail cuff with a Volume Pressure Recorder (VPR) and occlusion cuff measures blood pressure non-invasively. Rats with systolic or diastolic blood pressures over 129 or 90 mmHg are hypertensive.

Plasma is utilized to measure SOD activity. Start by gathering tools and materials at 18-25℃ room temperature. Place 50uL of standard and sample in each tube. Inject 50uL of sample diluent into each control well immediately. Add 100 uL HRP conjugate to each well and incubate at 37℃ for 60 minutes. Then, wash the microtiter four times. Add 50 uL of chromogen solutions A and B to each well. Mix for light protection and incubate at 37℃ for 15 minutes. Add stop solution to each tube and immediately take 450 nm readings for 15 minutes to determine plasma SOD levels.

White mice's orbital plexus vein blood was drawn into a tiny capillary tube, 2 ml per animal, and spun at 3000 rpm for 20 minutes at 4 °C to measure MDA levels. MDA is measured in red blood cell-separated serum. The exam is done on the same day as the blood draw. A spectrophotometric examination at 532 nm measured Thio Barbituric Acid Reactive Substance (TBARS) levels based on the red color change caused by the reaction generating

the thiobarbituric acid-MDA complex. The histopathological study uses paraffin to examine tissue cell morphology.

After treatment on the 28th day, animals were fixed with 10% formalin buffer and processed histologically with Hematoxylin Eosin (HE) staining. Each organ, the left and right kidney, was prepared and examined under a 400x microscope in five fields of view: the four corners and the center. The kidney's closing proximal tubule lumen is read. Testing materials can measure ureum from plasma, serum, or urine. After the experiment, a syringe drew five cc of blood through the heart. To collect serum for urea and creatinine measurement, the blood was centrifuged at 10,000 rpm for 10 minutes (Eppendorf 543R). A Hitachi UV/Vis® mouse instrument spectrophotometer read Randox® Kit ureum and creatinine results.

Rattus norvegicus, or male Wistar rats, were the subjects of the study. Aged two months, with a healthy weight of 150-200 grams and no visible abnormalities. Along with rabbits and monkeys, rats are commonly utilized as experimental animals. This is because, anatomically speaking, mice and humans are very similar. Wistar male white rats were employed in this study because their results are less affected by the menstrual cycle and pregnancy, making them a more reliable research subject. Additionally, researchers can more easily regulate rats' feeding and activity levels, reducing the possibility of bias [36].

With n being the sample size and t the sample group size, the Federer formula (n-1) (t-1) > 15 is used to find the sample size [37]. According to the results, at least six animals were in each treatment group. So, 24 people is the bare minimum for the sample size. Each treatment group included five animals, for a total of twenty-five used in the study. Each treatment group—P1, P2, and P3—received different amounts of EMBM (methanol extract of mango mistletoe). P1 received 75 mg/kgBW, P2 and P3 received 150 mg/kgBW, and P3 received 250 mg/kgBW, respectively. The control groups were negative and positive.

The tools used in this research are test animal cages measuring 40x30 cm, cage covers with woven wire, digital scales, sondes, rat drink bottles, digital scales, funnels, bottles, Petri dishes, beakers, blenders, ovens, freezers, rotary evaporator, paraffin block, surgical tools or 38 tattoos, mask, one med syringe, heating set, Eppendorf tube, tweezers and tissue hook, hand scoop, trash can (cracked), scissors, tweezers, needle for rat fixation, microcentrifuge, velvet satin fabric. The materials used in the research were male Wistar rats (Rattus norvegicus), test animal feed, rat drinking water and husks, mango mistletoe leaves (*Dendrophthoe pentandra*), 70% methanol, and label paper.

RESULTS

Male Wistar white rats (Rattus norvegicus) were separated into five groups for this study. The negative control group received no therapy or healthy mice. Positive control rats were given 1.5ml/kg prednisone and 25% NaCl to induce hypertension. The third group, treatment group 1, received conventional feed, water, and mango mistletoe extract 75mg/KgBW for 28 days. Fourth was treatment group 2, which received 150mg/KgBW mango mistletoe extract. Fifth, 250mg/KgBW mango mistletoe extract was given to group 3 (See Table 1).

Table 1. Characteristics Test Animals

Component	Treatment Group				
	K-	K+	P1	P2	P3
Types Rats	Rattus norvegicus				
Gender	Male				
General Condition	White fur, healthy and active				
Avg Initial BW (gram)	191	187	193	189	186
Avg Final BW (gram)	193	181	191	185	183

According to the data in Table 2, which shows that the average SOD levels varied, the highest rise in SOD levels was observed in treatment group 3, which consisted of mice exposed to DOCA-Salt and administered 250 mg/kg body weight of mango mistletoe extract (*Dendrophthoe pentandra*). In contrast, the treatment group saw a significant rise in SOD and MDA levels, while the positive control group—mice exposed to DOCA-Salt but only given distilled water—had the opposite effect.

By protecting cells from oxidative stress, SOD plays a key role. The antioxidant superoxide dismutase (SOD) has several roles in the body, according to research [28,30]. It protects cells from oxygen radical damage, reduces the production of inflammatory chemicals like prostaglandins, thromboxane,

and leukotriene, and inhibits DNA chain damage caused by superoxide. Plasma SOD activity measurements reveal this [28-29].

This study found that hypertensive rats significantly increased their SOD levels after receiving a dosage of mistletoe mango extract. Hypertension research needs to focus on increasing endogenous SOD levels as a potential treatment method.

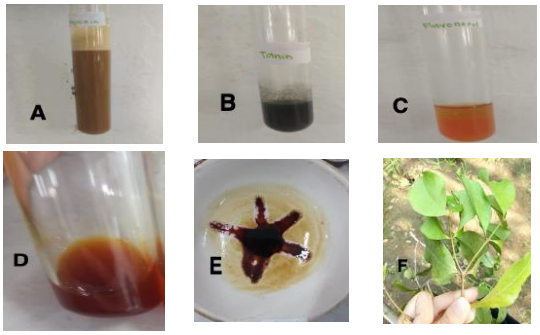
Mounting MDA causes DNA mutations, exacerbating existing diseases [30-31]. Researchers found that administering mango mistletoe extract to hypertensive rats reduced their MDA levels. Researchers found that measuring levels of malondialdehyde (MDA) in hypertensive rats both before and after administering mango mistletoe extract was an excellent way to gauge the extent to which the treatment affected the animals' cell membranes.

After comparing the average Ureum and Creatinine levels in Table 2, the researchers discovered that the third treatment group, which consisted of mice exposed to DOCA-salt and given 250 mg/kg body weight of mango mistletoe extract, had the most significant decrease in both markers, coming close to matching the control group. On the other hand, urea levels were least affected or improved in the positive control group, consisting of mice exposed to DOCA-salt but only given distilled water.

In breaking down proteins, urea is the primary by-product [42]. Blood contains ureum, a nitrogen molecule that is not a protein. The buildup of urea in the blood is a symptom of renal disease. When plasma urea levels rise, the kidneys aren't effectively filtering blood. Hemodialysis or kidney transplantation may be necessary for this potentially life-threatening condition [32-33]. This study showed that hypertensive rats given mango mistletoe extract had lower blood urea levels. Since the kidneys' ability to excrete urea is determined by the protein diet, it can be concluded that the treatment with mango mistletoe extract was effective.

Creatinine phosphate (protein), the result of muscle keratin metabolism, is produced in the liver, blood, and skeletal muscle [42]. The kidneys react with it to form urine. Unless a person has a significant physical injury or a degenerative condition that damages their muscles significantly, their daily creatinine formation should remain consistent [44]. The kidneys are responsible for filtering out creatinine, a byproduct of muscle metabolism, and excreting it in urine. This study's evaluation of the test animals revealed that hypertensive mice had lower keratin levels than the control group. Thus, as expected, keratinin levels have been reduced by using mistletoe mango extract.

Table 3. Phytochemical Test Results



Note: A. Saponins, B. Tannins, C. Flavonoids, D. Alkaloids, E. Triterpenoids, F. Mango mistletoe leaves

The phytochemical assays showed that mistletoe mango extract contains flavonoids, saponins, tannins, alkaloids, and triterpenoids (Table 3). For the saponin test (Figure A), 1 gram of mango mistletoe extract was placed in a test tube with 10 ml of hot water, cooled, and shaken violently for 10 seconds. Saponin is present if the foam is 1-10 cm high in 10 minutes and does not dissolve after adding one drop of 2 N HCl. This investigation discovered froth in the extract, indicating saponin.

Second, for the tannin test (Figure B), 1 gram of mango mistletoe extract is placed in a test tube, 10 mL of hot water is added, boiled for 5 minutes, and 3-4 drops of FeCl3 are added to the filtrate. Catechol tannin is present in blue-green (green-black). Blue and black indicate tannin. A blue-black liquid indicates tannin in tannin test findings.

The Three flavonoid test (Figure C). Concentrated HCl was added to 1 gram of mango mistletoe extract in a test tube and heated for 15 minutes in a water bath. Red or yellow indicates flavonoids (flavone, chalcone, and aurone). A yellow extract indicates the presence of flavonoids.

In the fourth alkaloid test (Figure D), 2 grams of mango mistletoe extract was placed in a test tube, dripped with 5 mL of HCl2N, heated, cooled, and divided into 3 1 mL test tubes. Reagents are added to each tube. If Mayer's reagent precipitates white or yellow,

alkaloids are present. In this study, the alkaloid test was red, indicating no alkaloids.

In the fifth triterpenoid test (Figure 5), mango mistletoe extract was added to a test tube with 2 mL of ethyl acetate and shaken. The ethyl acetate layer was dropped onto a drop plate to dry. After drying, two drops of acetic acid and one drop of concentrated sulfuric acid were added. Terpenoids are present if they become red or yellow. Steroids are present if they turn green. Red indicates triterpenoids in the steroid/triterpenoid test.

According to other studies, flavonoids (quercetin), saponins, and tannins are among the active compounds discovered in mango mistletoe. Quercetin is an aromatic ring compound with a hydroxyl group. Multiple studies show that secondary metabolite molecules like flavonoids can protect biological systems [19,35-36].

Table 2. Results of Measurements of SOD, MDA, Ureum, and Creatinine Levels

Group	Repitation	SOD		MDA		Ureum		Creatinine	
		Pra	Post	Pra	Post	Pra	Post	Pra	Post
Control –	1	13.2	13.6	2.2	2.5	16.1	16.7	2.9	3.1
	2	13.9	14.1	3.3	3.1	15.1	15.3	3.3	3.5
	3	12.9	13.2	2.5	2.7	15.7	16.1	4.3	4.2
	4	12.4	12.8	2.2	2.1	15.8	15.9	4.5	4.7
	5	12.1	12.2	3.3	3.5	16.4	16.5	2.6	2.8
	Mean	12.9	13.2	2.7	2.8	15.8	16.1	3.5	3.7
Control +	1	9.1	9.2	9.2	8.5	30.1	29.2	11.2	10.9
	2	9.9	10.1	8.8	7.9	31.4	30.1	11.9	10.2
	3	9.7	9.8	8.9	9.1	30.3	28.2	11.4	9.7
	4	9.2	10.5	8.6	8.9	28.9	28.6	10.9	9.2
	5	10.3	11.3	8.1	8.1	30.9	29.7	10.1	11.1
	Mean	9.6	10.2	8.7	8.5	30.3	29.2	11.1	10.2
Treatment P1	1	9.2	16.1	8.5	4.5	30.3	21.2	11.4	8.1
	2	9.3	16.6	9.9	4.9	31.5	22.1	12.1	7.9
	3	9.1	15.4	9.2	5.4	31.7	20.8	11.6	7.3
	4	9.4	17.3	8.3	5.8	30.5	21.5	10.9	8.2
	5	8.9	15.8	8.7	3.8	29.7	22.6	11.7	9.1
	Mean	9.2	16.2	8.9	4.9	30.7	21.6	11.5	8.1
Treatment P2	1	9.3	17.1	9.1	3.4	33.1	18.9	12.1	6.6
	2	8.9	16.8	8.7	4.1	29.7	19.1	11.3	6.1
	3	9.7	19.5	8.4	3.9	29.2	18.5	11.7	5.9
	4	9.1	17.7	9.5	4.7	32.1	18.2	10.7	7.2
	5	8.5	18.4	9.1	3.1	30.4	19.7	11.6	5.3
	Mean	9.1	17.9	9.0	3.8	30.9	18.9	11.5	6.2
Treatment P3	1	9.8	20.1	8.7	2.8	30.1	15.5	12.4	4.5
	2	8.2	19.2	8.8	2.2	32.4	16.4	11.2	3.3
	3	9.9	18.6	8.1	3.1	31.5	15.2	11.9	3.9
	4	8.6	19.9	9.5	3.8	28.4	16.7	10.8	5.5
	5	9.7	18.9	9.6	4.1	30.5	14.6	11.7	4.1
	Mean	9.2	19.3	8.9	3.2	30.6	15.7	11.6	4.3

Note: Pre-Test: After Exposure to DOCA-Salt (nmol/ml). Post-Test: After Administration of Mango Mistletoe Extract (nmol/ml). Group Control –: untreated group. They receive basic food and water. Group Control +: Induced 1.5 ml/kg prednisone and 25% NaCl were not given mango mistletoe extract. Treatment group 1: ordinary meal, water, and 75 mg/kg mango mistletoe extract. Treatment group 2: ordinary meal, water, and 150 mg/kg mango mistletoe extract, and Treatment group 3: ordinary meal, water, and 250 mg/kg mango mistletoe extract,

Table 5. Normality Test SOD, MDA, Ureum, and Creatinine Results

Groups		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
SOD Results	C -	.118	5	.200*	.996	5	.996
	C +	.142	5	.200*	.992	5	.986
	P-1	.175	5	.200*	.976	5	.912
	P-2	.173	5	.200*	.946	5	.707
	P-3	.208	5	.200*	.928	5	.584
MDA Results	C -	.159	5	.200*	.990	5	.980
	C +	.184	5	.200*	.944	5	.692
	P-1	.148	5	.200*	.985	5	.960
	P-2	.160	5	.200*	.979	5	.927
	P-3	.184	5	.200*	.967	5	.855
Ureum Results	C -	.167	5	.200*	.964	5	.833
	C +	.165	5	.200*	.968	5	.865
	P-1	.177	5	.200*	.974	5	.899
	P-2	.151	5	.200*	.982	5	.943
	P-3	.198	5	.200*	.951	5	.742
Creatinine Results	C -	.181	5	.200*	.953	5	.756
	C +	.203	5	.200*	.946	5	.708
	P-1	.251	5	.200*	.954	5	.763
	P-2	.166	5	.200*	.991	5	.984
	P-3	.191	5	.200*	.924	5	.554

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Table 6. Homogeneity Test SOD, MDA, Ureum, and Creatinine Results

		Levene statistic	df1	df2	Sig
SOD Result	Based on Mean	.485	4	20	.746
MDA Result	Based on Mean	.387	4	20	.815
Ureum Result	Based on Mean	.655	4	20	.630
Creatinine Result	Based on Mean	.216	4	20	.926

Table 7. One-Way ANOVA Test SOD, MDA, Ureum, and Creatinine Results

Result		Sum of Squares	df	Mean square	F	Sig
SOD	Between Groups	273.254	4	68.314	104.137	.000
	Within Groups	13.120	20	.656		
	Total	286.374	24			
MDA	Between Groups	105.652	4	26.413	61.944	.000
	Within Groups	8.528	20	.426		
	Total	114.180	24			
Ureum	Between Groups	606.478	4	151.620	303.847	.000
	Within Groups	9.980	20	.499		
	Total	616.458	24			
Creatinine	Between Groups	148.122	4	37.030	64.806	.000
	Within Groups	11.428	20	.571		
	Total	159.550	24			

Table 8. LSD Post-Hoc Test SOD, MDA, Ureum, and Creatinine Results

Dependent Variable : LSD Result		SOD Level		MDA Level		Ureum Level		Creatinine Level	
Group (I)	**Group (J)**	**Mean difference (I-J)**	**Sig**	**Mean difference (I-J)**	**Sig**	**Mean difference (I-J)**	**Sig**	**Mean difference (I-J)**	**Sig**
C+	C+	3.00000*	.000	-5.72000*	.000	-13.06000*	.000	-6.56000*	.000
	P1	-3.06000*	.000	-2.10000*	.000	-5.54000*	.000	-4.46000*	.000
	P2	-4.72000*	.000	-1.06000*	.018	-2.78000*	.000	-2.56000*	.000
	P3	-6.16000*	.000	-.42000	.321	.42000	.358	-.60000	.224
C-	C-	-3.00000*	.000	5.72000*	.000	13.06000*	.000	6.56000*	.000
	P1	-6.06000*	.000	3.62000*	.000	7.52000*	.000	2.10000*	.000
	P2	-7.72000*	.000	4.66000*	.000	10.28000*	.000	4.00000*	.000
	P3	-9.16000*	.000	5.30000*	.000	13.48000*	.000	5.96000*	.000
P1	C-	3.06000*	.000	2.10000*	.000	5.54000*	.000	4.46000*	.000
	C+	6.06000*	.000	-3.62000*	.000	-7.52000*	.000	-2.10000*	.000
	P2	-1.66000*	.004	1.04000*	.020	2.76000*	.000	1.90000*	.001
	P3	-3.10000*	.000	1.68000*	.001	5.96000*	.000	3.86000*	.000
P2	C-	4.72000*	.000	1.06000*	.018	2.78000*	.000	2.56000*	.000
	C+	7.72000*	.000	-4.66000*	.000	-10.28000*	.000	-4.00000*	.000
	P1	1.66000*	.004	-1.04000*	.020	-2.76000*	.000	-1.90000*	.001
	P3	-1.44000*	.011	.64000	.137	3.20000*	.000	1.96000*	.001
P3	C-	6.16000*	.000	.42000	.321	-.42000	.358	.60000	.224
	C+	9.16000*	.000	-5.30000*	.000	-13.48000*	.000	-5.96000*	.000
	P1	3.10000*	.000	-1.68000*	.001	-5.96000*	.000	-3.86000*	.000
	P2	1.44000*	.011	-.64000	.137	-3.20000*	.000	-1.96000*	.001

*. The mean difference is significant at the 0.05 level.

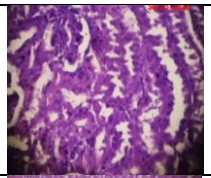
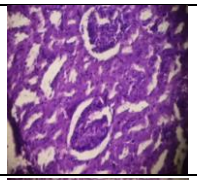
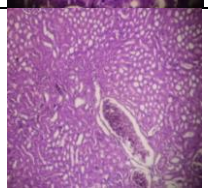
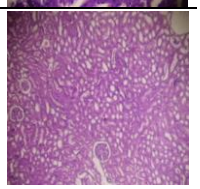
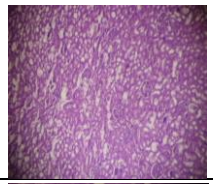
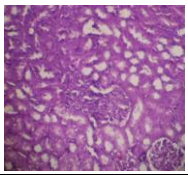
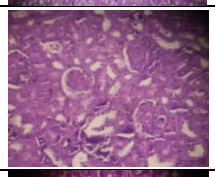
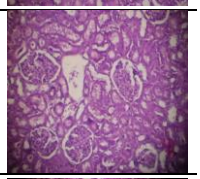
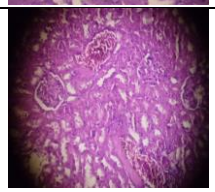
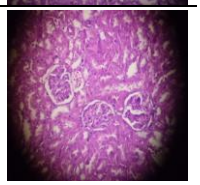
Note: C –: untreated group. They received basic food and water, C+: Induced 1.5 ml/kg prednisone and 25% NaCl were not given mango mistletoe extract, P1: ordinary meal, water, and 75 mg/kg mango mistletoe extract. P2: ordinary meal, water, and 150 mg/kg mango mistletoe extract, and P3: ordinary meal, water, and 250 mg/kg mango mistletoe extract,

Histopathological investigations were made with a 400x light microscope. This observation examined the cell structure and morphology of kidney tissue specimens from the control and treatment groups, using mango mistletoe extract at 75mg, 150mg, and 250mg/KgBW.

Histopathological observations (Table 4) demonstrate distinct cells. Histopathological preparations were assessed for quantitative data. Score 0 indicates no histopathological damage, Score 1 is focal (mild), Score 2 is multifocal (moderate), and Score 3 is diffuse (severe) [47].

The negative control group fed ordinary pellets and distilled water had normal kidney histology and scored 0. Due to their lack of DOCA-Garam exposure, the negative control group's kidney histology was normal. Thus, it was utilized to describe the other groups and compare them to the treatment group that received mango mistletoe extract. Due to DOCA-salt ingestion, the positive control group's kidneys displayed different histological structures. Damaged kidney histology scored this group in category 3 (diffuse/severe damage). Group 1 received 75mg/KgBW mango mistletoe extract and saw kidney histological improvement, but there was still multifocal/moderate damage. Therefore, it was scored in category 2. Group 2 received 150mg/KgBW mango mistletoe extract and improved, but it still has focused or mild harm; thus, it is in scoring category 1. Treatment group 3 received 250mg/KgBW DOCA-Salt and mango mistletoe extract and had a kidney histological structure similar to the control group. Hence, it was scored 0.

Table 4. Histopathological Results

Groups	Histopathological Image of Kidney Tissue	
	Pre-Test	Post-Test
Control Negative (C -)		
Control Positive (C +)		
Treatment I (P-1)		
Treatment II (P-2)		
Treatment IIII (P-3)		

Note: Pre-Test: After Exposure to DOCA-Salt (nmol/ml). Post-Test: After Administration of Mango Mistletoe Extract (nmol/ml). C-: untreated group. They receive basic food and water, C+: Induced 1.5 ml/kg prednisone and 25% NaCl and were not given mango mistletoe extract, P1: ordinary meal, water, and 75 mg/kg mango mistletoe extract. P2: ordinary meal, water, and 150 mg/kg mango mistletoe extract. P3: ordinary meal, water, and 250 mg/kg mango mistletoe extract,

In male Wistar white rats (Rattus norvegicus) subjected to DOCA-Garam, mango mistletoe extract at 150mg/KgBW and 250mg/KgBW improved kidney histology. Because it is closer to the usual group, 250mg/KgBW works better—histopathological studies of the kidneys in control and treatment group 3 show similar morphologies. Mango mistletoe extract compounds improve the kidney organ histology of male Wistar white rats (Rattus norvegicus) subjected to DOCA-Garam.

Quercetin, a flavonol molecule of the flavonoid class, is an antioxidant component contributing to mango mistletoe. The hydroxyl group in quercetin inhibits lipid peroxide, making it capable of capturing free radicals. Quercetin can enhance superoxide dismutase (SOD) activity and bind to free radicals [19,35-36]. Histological analysis of the kidneys of rats with hypertension reveals that mango mistletoe's antioxidant components improve kidney function.

Due to the small sample size (<30), the Kolmogorov-Smirnov test was utilized for the normalcy test in this investigation [35]. The significance of data normality testing lies in that data is believed to represent the population when it follows a normal distribution. The data is said to be regularly distributed if the p-value is more significant than 0.05 and not normally

distributed if the p-value is less than 0.05. In all groups, the results of the normality test on SOD, MDA, Ureum, and creatinine levels were 0.200, as shown in Table 5. Since the p-value is more significant than 0.05, we may conclude that the data in this study follows a normal distribution.

Using a 5% significance threshold, the Levene test was used to assess for group homogeneity. As a rule of thumb, while making decisions, a significance value less than 0.05 indicates that the data is not homogeneous. In contrast, a significance value of more than 0.05 suggests that the data is homogeneous [35]. All four of the following significance values are more significant than 0.05: SOD (0.746), MDA (0.815), Urene (0.630), and Karatenin (0.926)—these values are shown in Table 6, which displays the results of the homogeneity test with the probability value in the significance column. It follows that all study groups are representative of similarly distributed or homogeneous populations.

After ensuring that the data was normal and homogenous and that the findings followed a normal distribution with a constant variance, the researchers ran a one-way ANOVA to see whether there was a statistically significant difference in the performance of the groups [35]. The findings of the One-way ANOVA can be seen in Table 6, which indicates that the levels of SOD, MDA, Urene, and Karatenin had significance values of 0.000 or less than 0.05. From these numbers, we can deduce that the treatment group differs significantly from the control group, suggesting that a factor with a finite number of levels influences the dependent variable [35].

A post-hoc LSD test was performed to compare the group's average SOD levels. A significance value below 0.05 indicates substantial differences between groups and vice versa [35]. Whether groups differ significantly is determined by the LSD Post Hoc Test. The SOD level analysis (Table 8) shows a significant difference between the negative control group and the positive control group (p= 0.000), treatment groups 1 and 2, and treatment groups 3 (p= 0.000).

MDA levels (Table 8) demonstrate a significant difference between the negative control group, positive control group, treatment group 1 (p= 0.000), and treatment group 2 (p= 0.018). No difference was seen between negative control and treatment group 3 (p= 0.321). Similarly, urea levels (Table 8) differ significantly between the negative control group and the positive control group (p= 0.000), treatment group 1 (p= 0.000), and treatment group 2 (p= 0.018). No difference was seen between negative control and treatment group 3 (p= 0.358).

Keratin levels (Table 8) demonstrate a significant difference between the negative control group, positive control group, treatment group 1 (p= 0.000), and treatment group 2 (p= 0.018). No difference was seen between the negative control and treatment group 3 (p= 0.224).

DISCUSSION

Many free radicals in the body generate an imbalance between antioxidant production and incoming free radicals [5]. We term this imbalance oxidative stress. The reactivity of ROS, which can damage DNA, proteins, and lipids in cells, reduces SOD levels in response to oxidative stress. Free radicals accumulate and cause necrosis and apoptosis when SOD and other enzyme antioxidants diminish.

The etiology of hypertension involves endothelial cell oxidative stress and inflammation, which cause high mortality and morbidity [4]. Oxidative stress increases cardiovascular disease and its consequences, including hypertension [5-6].

The researchers hypothesize that mango mistletoe extract increases SOD levels and improves renal function in male Wistar white rats (Rattus norvegicus) exposed to DOCA-Garam. Male Wistar white rats (Rattus norvegicus) were tested to confirm this suspicion.

Quercetin derivates from flavonoids are found in mango mistletoe's phenol, routine, tannin, and meso-inositol groups [46]. Multiple studies show that manganese mistletoe can treat many ailments, including hypertension. Mango mistletoe contains flavonoid derivatives such as quercetin, phenols, routine, and tannins [45]. Quercetin releases hydrogen ions to peroxy free radicals during propagation and initiation, making them more stable and preventing oxidation [29].

DOCA-Salt induced hypertension in test animals to start this study. Salt and DOCA raised blood pressure in this animal test. DOCA-induced male Wistar rats subcutaneously. DOCA increases blood vessel LDL buildup, causing blockages and

hypertension. DOCA, an adrenal gland steroid hormone, is a mineralocorticoid and precursor of aldosterone. The adrenal zone glomerulosa produces most aldosterone.

This 28-day research approach produced data that needed to be processed and assessed; therefore, normality, homogeneity, and significance tests were required. The Kolmogorov-Smirnov test in SPSS determined normality. Thus, all SOD, MDA, urea, and creatinine test groups had normally distributed data with a significance value of 0.200. Thus, the data is regularly distributed or represents the population.

Ureum and creatinine data were then analyzed for homogeneity using the Levene test to check if the population had the same variance. SOD, MDA, urea, and creatinine levels had significance values of 0.746, 0.815, 0.630, and 0.926, respectively. A significant probability value larger than 0.05 indicates that SOD, MDA, urea, and creatinine levels in all groups are homogeneous or from the same population. One-way ANOVA assessed this normally distributed and homogeneous data for efficacy and significance.

The One-way ANOVA test on SOD, MDA, urea, and creatinine levels yielded 0.000 or greater than 0.05. Based on this data, a follow-up post-hoc LSD test is needed because the control group, treatment group 1, treatment group 2, and treatment group 3 differ significantly. A post-hoc LSD test was used to compare the group's average urea and creatinine levels.

The LSD Post Hoc Test examination of SOD levels demonstrated significant differences between the negative control group and the positive control group (p= 0.000), treatment groups 1 and 2, and treatment group 3.

The LSD Post Hoc Test examination of MDA levels demonstrated a significant difference between the negative control group, positive control group, treatment group 1 (p= 0.000), and treatment group 2 (p= 0.018). No difference was seen between negative control and treatment group 3 (p= 0.321).

A significant difference in Ureum levels was found between the negative control group and the positive control group (p= 0.000), treatment group 1 (p= 0.000), and treatment group 2 (p= 0.018). No difference was seen between negative control and treatment group 3 (p= 0.358). Creatinine levels differed significantly between the negative control group, positive control group, treatment group 1 (p= 0.000), and treatment group 2 (p= 0.018). No difference was seen between the negative control and treatment group 3 (p= 0.224). This investigation shows that treatment group 3, administered mango mistletoe extract at 250mg/KgBW, had MDA, Ureum, and creatinine levels similar to the negative control group and healthy mice.

The kidneys of tested mice were examined histologically. In male Wistar white rats (Rattus norvegicus) subjected to DOCA-Garam, mango mistletoe extract at 150mg/KgBW and 250mg/KgBW improved kidney histology. Because it is closer to the usual group, 250mg/KgBW works better—histopathological studies of the kidneys in control and treatment group 3 show similar morphologies. Mango mistletoe extract compounds improve the kidney organ histology of male Wistar white rats (Rattus norvegicus) subjected to DOCA-Garam.

According to phytochemical assays, the mistletoe mango extract contains flavonoids, saponins, tannins, and triterpenoids. This study's mango mistletoe extract content matches with another researcher [19, 35-36]. This study discovered mango mistletoe extract's flavonoid, saponin, and tannin components.

Mango mistletoe flavonoids can heal hypertension-damaged kidneys. Plant flavonoids have antioxidant, antiapoptotic, and anti-inflammatory effects. Flavonoids decrease excess reactive oxygen species, boost antioxidant status, and mediate antioxidant responses, protecting the kidneys. Flavonoids control inflammatory indicators, reduce inflammation, and protect kidney cells from apoptosis [19, 35-36].

CONCLUSION

Lifestyle choices, genetics, and other medical issues are among the many potential causes of hypertension. This study used mango mistletoe extract to examine the effects on hypertensive rats. Researchers found that white Wistar rats (Rattus norvegicus) exposed to DOCA-Garam had their SOD levels increased by 250 mg/kg body weight of mango mistletoe extract. Evidence suggests that superoxide dismutase (SOD) can shield cells from oxidant stressors, also known as free radicals.

SOD is a main line of defense against oxidative stress since it breaks down superoxide anions into H2O and peroxide. The lowest levels of malondialdehyde (MDA) relative to the other groups in treatment three further demonstrated that MDA was an effective marker of cellular abnormalities induced by free radicals.

Treatment group 3 also had lower Ureum levels than the other groups, according to the results. It follows that mango mistletoe extract can mitigate the effects of consuming too many high-protein foods by lowering urea levels.

Results showed that treatment 3 had the lowest Creatinine levels compared to the other groups, suggesting that the hypertensive rats' kidneys benefited from the mango mistletoe extract's ability to lower Creatinine levels.

The histological examinations of kidney tissue in the third treatment group, which received 250 mg/kg body weight of mistletoe mango extract, showed the maximum recovery and were very close to those in the control group.

This leads us to believe that the secondary metabolites found in mango mistletoe extract, such as tannins, saponins, flavonoids, and triterpenoids, aid in the restoration of damaged kidney cells and the elevation of superoxide dismutase (SOD) levels, both of which are consequences of hypertension.

This study's findings may provide light on whether or not hypertensive patients benefit from taking mango mistletoe extract to boost superoxide dismutase (SOD) levels and enhance kidney function. Additionally, additional studies are required to determine the safety and efficacy of mango mistletoe extract when administered to human subjects.

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