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Histopathological Profile of Therapeutic Doses of Mango Mistletoe Methanolic Extract (MMME) in Cardiac of Hypertensive Rats (DOCA-Salt)

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Abstract: The aim of this study was to determine the histopathological profile of the cardiac in hypertensive rats (DOCA-Salt) treated to Mango mistletoe Methanolic Extract (MMME) for 14 days using the true experimental design method with completely randomized design on 50 rats, divided into 5 treatments, namely control (-) , control (+), treatment 1 dose 50 mg / KgBB, treatment 2 doses 100 mg / KgBB and treatment 3 doses 200 mg / KgBB with replication 5 times. One way ANOVA analysis was used, namely JAMOVI with version 1.1.9.0 and for the calculation of cell diameter using the IMAGE J application. The results showed that the histopathological profile of the cardiac in hypertensive rats (DOCA-Salt) treated to MMME for 14 days on the diameter of the heart muscle cells did not significant difference between the control (+) and control groups (-), treatment 1, 2, and 3. This is evidenced by the results of the analysis of p-value> 0.05, namely 0.187, so we concluded that MMME does not affect the diameter of heart/cardiac organ muscle cells. However, there was a very significant difference in the amount of necrosis in the cardiac of hypertensive rats between the control (+) and control (-) groups, treatment 1, 2, and 3. This was evidenced by the results of the analysis showing a p-value <0.05, namely <0.001, so it can be concluded that MMME can reduce the number of necrosis in the heart/cardiac organ.

Keywords: Hypertension, Methanolic Extract, Mango Benalu, Cardiac Histopathology, DOCA-salt

1. Introduction

Indonesia is very rich in biodiversity (Biodiversity), and is known as the country with the second largest biodiversity in the world after Brazil, which consists of tropical plants and marine biota. There are about 30,000 types of plants and 7,000 of them have medicinal properties, but only 2,500 have been used as medicinal plants [12].

Among the examples of medicinal plants is the mango parasite (*Dendropthoe petandra*). From the results of previous research, *Dendrophthoe pentandra* extract was known to have antiplasmodium activity [15]. Mango seedling also has the potential as an anti-colon cancer agent [37]. Meanwhile, based on other research, it is known that mango parasite extract can reduce cholesterol and LDL levels [33].

The active substances contained in mango parasites include: flavonoids, amino acids, carbohydrates, tannins, saponins, and alkaloids [21]. Other studies have shown that mango parasites also contain active substances such as flavonoids (quercetin), saponins and tannins [22]. Benalu mangoes are included in vascular plants, in which there are phenol group compounds or better known as flavonoid compounds [2].

Mango mistletoe (*D. pentandra*) is widely used in the traditional medical world. In Malaysia, this parasite is used to stop roundworm infection in children [34]. In addition, it is also used to treat coughs, hypertension, diabetes, cancer, stomach ulcers, measles, diuretics, skin infections, and postpartum conditions [3, 26, 39,1] and has the potential to be developed into an immunomodulator [1]. Therefore, mango parasite leaves can be developed into standardized traditional medicine.

Hypertension therapy is divided into two, namely non-pharmacological and pharmacological therapy. The non-faculty therapy is to use it as a phytopharmaca product for alternative natural antihypertensive drugs. Based on research by numbering [32] flavonoid compounds in parasites are known to have anticancer activity, namely quercetin. Quercetin is a flavanol molecule found in mango parasites [19]. Antioxidants play an important role in the mechanism of quercetin compound namely at the initiation stage quercetin is able to stabilize free radicals produced by carcinogenic compounds such as oxygen radicals, peroxide and superoxide [17]. Quercetin can stabilize carcinogens such as oxygen radicals, peroxide and superoxide through hydrogenation reactions and complex formation [30]. Through this reaction, free radicals are converted into a more stable form so that they are unable to oxidize DNA.

2. Research Method

This research was conducted after obtaining approval from the Research Ethics Commission of the Faculty of Medicine, Islamic University of Malang (*Ethical Clearance* with No. 006 / LE.001 / IV / 03/2020. This study used an experimental method with a completely randomized design study (CRD). MMME was exposed to male Wistar rats (*Rattus norvegicus*) for 14 days and clinical biochemical examination of heart function and histopathological observations of male Wistar rats were carried out.

This research is a true experimental design with completely randomized design on 50 rats with 3 treatments, 1 positive control and 1 negative control. Each treatment had 5 replications. Using 5 repetitions it has been described in the [8] that each treatment dose uses at least 5 repetitions. The subjects of this study were using male wistar rats (*Rattus norvegicus*) because they have sensitivity, metabolism of the test preparation similar to humans, in which the male sex was exposed to the MMME test preparation for 28 days (subchronic) with the aim of clinically testing the dosage in a single-use form. and repeatedly for less than 1 week [8].

This research was conducted in June - October 2020 at the Animal House Laboratory, Faculty of Mathematics and Natural Sciences, Islamic University of Malang, Ecology Laboratory, Faculty of Mathematics and Natural Sciences, Islamic University of Malang, Central Laboratory of

the Faculty of Mathematics and Natural Sciences, Islamic University of Malang, Anatomical Histopathology Laboratory Brawijaya University, Laboratory of Balai Materia Medica Batu, East Java, and Laboratory of the Faculty of Medicine, Islamic University of Malang.

The tools and materials used are the test animal cage measuring 40x30 cm, cage cover with woven wire, digital scales, husks (for mouse mats), rat drink bottles, digital scales, funnel, bottles, measuring cups, erlenmeyer, blender, oven, freezer. , rat dissection board, mask, one med spluit, heating set, efendorf tube, tweezers, tissue hook, handscoon, trash can, scissors, tweezers, needle for fixation of mice, microsentrifuge, vaplet. Materials needed are feed and drinking water for rats, mango parasite leaves (*Dendrophthoe pentandra*) and 96% methanol, ether anesthesia, female white rats (*Rattus norvegicus*) 6-8 weeks old, with a body weight of 200-300 grams, ketamine for anesthesia, PBS (*Phosphate Buffered Saline*) solution, and formalin.

Test Animal Acclimatization Process

The animal used in this study was the male white rat rodentia. Rats were acclimatized in the Animal House Laboratory of the Faculty of Mathematics and Natural Sciences, Islamic University of Malang for 1 week with a room temperature of ± 240C with an air humidity of approximately 50-60% protected from industrial fumes and other pollutants and given food and drink. On the seventh day of acclimatization, the rats weighed which were considered as the preconditioned body weight and continued until the treatment period for 7 days.

Preparation of Mango Mistletoe Methanolic Extract

The leaves of mango parasite (*Dendrophthoe pentandra*) were obtained from Kepanjen City Malang and were determined in the Laboratory of Balai Materia Medica Batu, East Java. The leaves used are dry simplicia leaves that are clean and not rotten. Each parasite leaf is heated at 400-600 until the water content of the parasite leaves is lost. We weigh the wet weight and dry weight of parasites. Once dry, then cut the leaves until crushed. Then it is mashed by blending to form a powder (powder simplicia) [4].

Extraction of parasites using the maceration method. The extraction was initiated after the powder simplicia was formed, each mango parasite leaf was weighed 100 grams and then put into a 1.5 liter bottle. The powder simplicia was soaked in 1 liter of 90% methanol and was shaken for 60 minutes until the solution was homogeneous. After that, the shaken simplicia powder is allowed to stand for 24 hours with the aim of breaking the mango parasite leaf cell walls and the active substance in the leaves can be withdrawn by the methanol solvent. The rest of this immersion for 24 hours will form two layers, with the top layer called supernatant and the bottom layer in the form of natant. This supenatant will be accommodated and followed by the extraction stage using a rotary evaporator. Supernatant is an active ingredient in mango parasite leaves in methanol solvent [4,5].

The mango parasite leaf powder was extracted using the maceration method with methanol as a solvent. In the maceration process, the sample undergoes a breakdown of the cell wall and cell membrane due to the difference in pressure between inside and outside the cell so that the secondary metabolites in the cytoplasm are dissolved in the solvent or a diffusion process occurs [20]. The use of methanol as a solvent in the maceration process is because this solvent can dissolve almost all secondary metabolite compounds. Other studies have shown that methanol is able to isolate more secondary metabolites for phenolic compounds, flavonoids and tannins. The leaves of mango parasites contain polar chemical compounds, namely flavonoids, so to extract these compounds using a solvent that is also polar, namely methanol. In addition, methanol has a relatively low boiling point so it is easily evaporated. The use of solvents with different levels of polarity affects the type of compound extracted.

3. Maintenance of Experimental Animals

Male wistar rats are kept and put in their cages at the Animal House, Faculty of Mathematics and Natural Sciences, Islamic University of Malang. Then given food and drink according to laboratory standards. Before the experiment started, the animals were acclimatized for approximately seven days. After being acclimatized, the experimental animals were weighed for the determination of the EMBM dose. Weighing the body weight of experimental animals was carried out once a week to determine the volume of the dose given.

Provision of Mango Mistletoe Methanolic Extract

MMME was given for 14 days. Each week the rats were weighed to determine their body weight and set the dose to be given. In male Wistar rats, the first dose with the first treatment (PI) was 50 mg / kgBB, the second dose with the second treatment (PII), which was 100 mg / kgBB, and the third dose with the third treatment (PIII), namely 200 mg / kgBB. Each treatment contained 5 mice as repetitions. The treatment was carried out on each mouse according to the given dose and volume using a rat swab.

Test Animal Surgery

After 28 days of rearing and treatment of male Wistar rats, surgery was carried out and blood samples were taken according to the order of treatment. Each male Wistar rat was anesthetized with ketamine, waited until fainting and then operated vertically from the abdomen to the thorax using scissors section until the entire abdomen was exposed.

Histopathological Examination

The cardiac organs were placed in a KCl & PBS buffer 25 mM, then stored in 40% neutral buffered formaldehyde at room temperature. Hematoxylin and eosin (H&E) (~ 5µm) portions were prepared for histopathological measurement. Parts were photographed at 400x magnification using Olympus (Tokyo, Japan). Microscope exposure, focus, and plane selection are optimized for differentiating cell boundaries. The image is opened and after setting the threshold, it is analyzed. Data from all fields are combined and then analyzed.

Analysis Data

Data obtained from the Laboratory of Anatomical Histopathology, Universitas Brawijaya Malang, all data for each group were entered in the table and were subjected to statistical tests using the SPSS (*Statistical Product and Service Solution*) computer program using the Jamovi application version 1.1.9.0.). Significant differences between means were analyzed using the statistical one-way analysis of variance (*ANOVA*) method and followed by Duncan's test to differentiate between the control and treatment groups ($p < 0.05$). The test used is the one-way analysis of variance (*ANOVA*) test which aims to compare the mean difference of more than 2 treatments with a 95% confidence level.

3. Result and Discussions

3.1 Result Histopathological Observation of Heart Necrosis

After observing the histopathological anatomy of cardiac necrosis in hypertensive male Wistar rats (*Rattus norvegicus*) (DOCA-Salt) exposed to Mango Mistletoe Methanolic Extract (MMME), the results were tabulated based on the treatment of each group presented in the form of a histogram as follows .

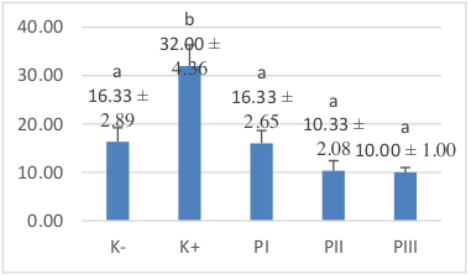

Figure 1.Histogram of Average Number of Heart Necrosis in Hypertensive Rats (DOCA-Salt) Exposed to Mango Mistletoe Methanolic Extract (MMME).

Information :

K- = Negative Control

K + = Positive Control
PI = Treatment 1 (50mg / KgBB)
PII = Treatment 2 (100mg / KgBB)
PIII = Treatment 3 (200mg / KgBB)

Based on the results of the *One Way ANOVA* test ($p < 0.001$), all treatments P1, P2, and P3 were significantly different from the control.

The results of the analysis of the histopathological anatomical observations of heart necrosis in hypertensive male Wistar rats (*Rattus norvegicus*) (DOCA-Salt) exposed to Benalu Mango Methanolic Extract (MMME), showed that there were very, very significant differences in all groups, especially between positive control groups (K +). with negative control groups (K-), treatment 1, 2, and 3. This is evidenced by the results of the *One Way ANOVA* test that ($p < 0.001$), that is, there is a very very significant difference between K + (inducer) and the K- and all treatment groups were given MMME for 14 days with different doses, namely PI (50 mg / KgBB), P2 (100 mg / KgBB), and P3 (200 mg / KgBB). So it can be interpreted that exposure to Mango Mistletoe Methanolic Extract (MMME) for 14 days can reduce the mean number of necrosis in the heart organs of hypertensive rats (DOCA-Salt). The three dose variations have the same potential in reducing the number of necrosis of cells in the heart (left ventricle), which are indicated by (a) which indicates that there is no significant difference between the three dose variants in reducing the number of necrosis in the heart organ. However, the most optimum dose is the second dose, namely P3 (100 mg / KgBB) because it can reduce the mean number of necrosis in the heart organ, especially the left ventricle, lower than the K-value.

Based on the histogram image above, it shows that there is a very, very significant difference between the K + group and all treatment groups. A very significant difference was indicated by the mean number of necrosis of 32.00 cells, whereas in all treatment groups the mean value of necrosis was between 16.33 - 10.00 cells. Therefore, on the histogram the sign of significance is indicated by (b) which means that it has very, very significant differences between the K + groups with K-, P1, P2, and P3.

3.2 Observation Results of Histopathological Anatomy of Heart Necrosis

Cell damage (necrosis) is affected by several diseases, one of which is hypertension, which can change the structure and tissue of cells, resulting in a fatal possibility, namely cell death. Necrosis usually consists of three phases namely pycnosis, caricorrection, and cariolysis. The description of the histopathology of heart cell necrosis (left ventricle) anthomy in hypertensive rats (DOCA-Salt) exposed to mango parasite methanolic extract (MMME) for 14 days is as follows:

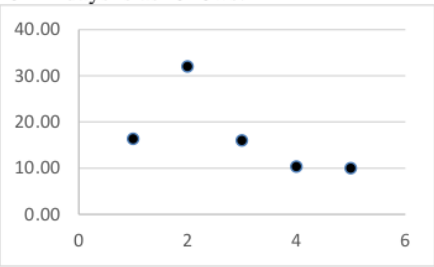

Figure 2.Histopathological Overview of the Heart (left ventricle) of Hypertensive Rats (DOCA-Salt) Exposed to MMME for 14 Days in the Positive Control Group.

Table 1. Results of Calculation of Cardiac Necrosis in hypertensive rats (DOCA-Salt) exposed to Mango Mistletoe Methanolic Extract (MMME).

No.	Heart Necrosis(Cell)				Average ± SD
	Treatment	1	2	3	
1.	K-	18	18	13	16.33 ± 2.89[a]
2.	K+	37	30	39	32.00 ± 4.36[b]
3.	PI	19	14	15	16.00 ± 2.65[a]
4.	PII	8	12	11	10.33 ± 2.08[a]
5.	PIII	11	9	10	10.00 ± 1.00[a]

Based on the cardiac histopathological picture in the left ventricle of hypertensive rats (DOCA-Salt) exposed to Mango Mistletoe Methanolic Extract (MMME) for 14 days, it shows that there are signs of necrosis (cell damage) due to exposure to the hypertension model using *Deoxycorticosterone acetate* (DOCA) at a dose 15 mg / KgBB and 2% NaCl. In Figure 5.2 above is a heart histopathological picture of the positive control group, there is necrosis (cell damage) in the heart (left ventricle) in an average number that is relatively more necrosis than the normal mean number of cells. This is shown by the black circle, that necrosis consists of three types, namely pycnosis, cariorexis, and cariolysis. Fig. 2 also shows the presence of inflammation induced by exposure to DOCA-Salt as a model of hypertension. Inflammation is also caused by free radicals in the body which will also have an impact on increasing the number of cell necrosis, especially in the heart organ (left ventricle).

3.3 Results of Measurement of Heart Organ Cell Diameter (Left Ventricle)

After measuring the diameter of heart cells (left ventricle) in hypertensive male Wistar rats (*Rattus norvegicus*) (DOCA-Salt) exposed to Benalu Mango Methanolic Extract (MMME), the results were tabulated based on the treatment of each group presented in the form of the histogram as follows.

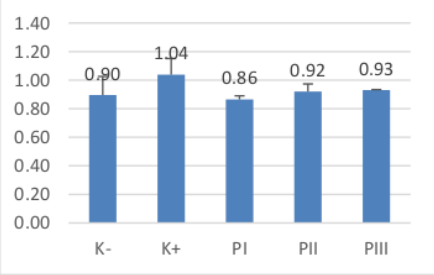

Figure 3.Histogram of Average Heart Cell Diameter Measurement (left ventricle) in Hypertensive Rats (DOCA-Salt) Exposed to Benalu Mango Methanolic Extract (MMME).

Information :
K- = Negative Control
K + = Positive Control
PI = Treatment 1 (50mg / KgBB)
PII = Treatment 2 (100mg / KgBB)
PIII = Treatment 3 (200mg / KgBB)

Based on the results of the One Way ANOVA test (p> 0.001), all treatments P1, P2, and P3 were not significantly different from the control.

Based on the histogram image above, it shows that there was no significant difference between the K + (inducer) group and all treatment groups. The insignificant difference was indicated by the mean number of cells in the K + group (inducer), which was 1.04 μm, whereas in all treatment groups the mean cell diameter was between 0.83 - 0.93 μm. Therefore, on the histogram the sign of significance is indicated by (a) which means that there is no significant difference between the K + groups and the K-, P1, P2, and P3 groups. However, indirectly giving the hypertension model (DOCA-Salt) can widen the diameter of the heart muscle cells although it is not significant, this is because the response to increased blood pressure in chronic hypertension causes specific structural and functional changes [11]. Our hypertensive mouse model is characterized by left heart remodeling. Characteristics include an increase in the diameter of cells in the left ventricular heart organ, the thickness of the left ventricle wall which shows an increase in echocardiogram images, while the shortening of the left ventricular fraction and decreased ejection fraction. Histological observations identified an enlarged diameter of the cardiomyocytes. The presence of left ventricular hypertrophy (LVH) and cardiac dysfunction are common complications of arterial hypertension, and as indicators of end organ damage [35].

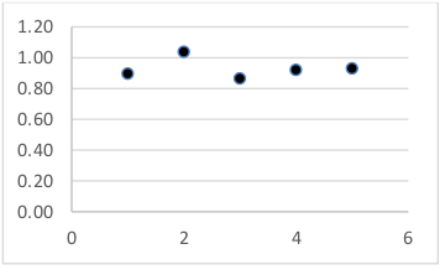

Figure 4.Histopathological Overview of Heart (left ventricle) Hypertensive Rats (DOCA-Salt) Exposed to MMME for 14 days a.) Control (-) b.) Control (+) c.) Treatment 1 d.) Treatment 2 e.) Acknowledgment 3.

Based on observations of cell diameter measurements in the cardiac histopathological picture in the left ventricle of hypertensive rats (DOCA-Salt) exposed to Mango Mistletoe Methanolic Extract (MMME) for 14 days, it showed that there was no significant difference in the group exposed to the hypertension model using *Deoxycorticosterone acetate* (DOCA).) with a dose of 15 mg / KgBB and NaCl 2% in this case is a positive control group with all treatment groups and negative controls. In Figure 4. above is an overview of cardiac histopathology in all groups, it can be seen that the cell diameter between the control groups, both negative and positive, and all treatment groups, has no significant difference. This is as shown in the figure above, that the diameter between all groups is not a significant difference as in the results of the previous analysis. Thus, it indicates that there is hypertrophy in the heart of the left ventricle of the rats exposed to the hypertension model using *Deoxycorticosterone acetate* (DOCA) at a dose of 15 mg / KgBB and NaCl 2% is not too severe, and the administration of mango parasite methanolic extract is very effective in reducing hypertrophy levels in left ventricle part of the heart.

In this case, traditional Indonesian medicine can inhibit left ventricular hypertrophy and left ventricular dysfunction through the mechanism of NADPH oxidase which can inhibit the formation of oxidative stress. Mango parasite methanolic extract (MMME) may inhibit cardiac hypertrophy through a mechanism that may involve reducing the formation of oxidative stress produced by the NADPH oxidase pathway. Treatment using MMME can efficiently lower blood pressure and reverse ventricular remodeling in hypertension. This mechanism may be related to the inhibitory effect of MMME on the formation of ROS via the cardiac NADPH oxidase pathway. This study also showed an increase in cardiac endogenous antioxidant levels with MMME administration. Therefore, these findings can provide a theoretical basis for using MMME in the treatment of hypertension and its myocardial hypertrophy. MMME may be new candidates for cardioprotective drugs for patients with hypertensive vascular disease. These findings should be important for advances in preclinical and clinical research.

Discussions

The mango parasite (*Dendrophthoe pentandra* L. Miq.) Is one of the parasites that is easily available in Indonesia because most of the Indonesian region is lowland where mango trees are very suitable for living in the lowlands [29]. The mango parasite plant used by the community as traditional medicine or known as jamu needs to be reviewed. This is because according to the POM there are several traditional medicines that are no longer used for treatment because they have unwanted effects. In addition, natural medicines may contain toxic compound properties [6]. According to research by numbering [2] states that a number of medicinal plants containing flavonoids have been reported to have antioxidant, antibacterial, antiviral, anti-inflammatory, allergy and anti-cancer activities, including mango parasites. Benalu is one of the promising plants and still needs further exploration. Apart from being used in traditional preparations (herbal medicine), parasites also have the opportunity to be used as phyto-pharmacy [2].

In this study, the aim of this study was to determine the analysis of histopathological anatomical necrosis observation and measurement of the diameter of heart cells in hypertensive rats (DOCA-Salt) exposed to Mango Mistletoe Methanolic Extract (MMME) for 14 days subchronic. The results of the study based on the histogram showed that the negative control group (K-) histopathological observation of heart necrosis was 16.33, while the positive control (K +) was 32.00, at P1 16.00 and P2 was 10.33, and in the P3 group the mean number of necrosis was 10.00. Analysis of Histopathological

Anatomical Observation of heart cell necrosis in hypertensive rats (DOCA-Salt) exposed to Mango Mistletoe Methanolic Extract (MMME) for 14 days showed an increase in the positive control group and a decrease in each treatment group when compared to controls. Based on the results of the analysis of histopathological observations of heart cell necrosis, it shows that exposure to mango parasite methanolic extract (MMME) for 14 days with a multi-level dose variant is effective in reducing the number of cell necrosis in the heart organ of hypertensive rats (DOCA-Salt). There was a significant reduction in all groups in each treatment. The results of statistical tests on the three dose variations did not show any significant differences, the ability of mango parasite methanolic extract (MMME) to affect the number of heart cell necrosis was relatively the same, and symbol a found in all treatments stated that the results of the study on the histopathology of heart cell necrosis of male rats *Rattus norvegicus* was not significantly different from control. Meanwhile, symbol b shows a real or significant difference between the positive control group and all treatment groups.

One of the histopathological observations is observing cell damage (necrosis). Necrosis is cell death. Necrosis can be focal (central, middle, peripheral) or massive. Usually, necrosis is acute [24]. The characteristic of necrosis is the appearance of necrotic heart muscle fragments or cells without nuclear outlay or no cells appear to be accompanied by an inflammatory reaction. Whether or not the remaining heart cells are visible depends on the duration and type of necrosis [7]. Necrotic cell death is the death of cells that are still alive, if strong stimulation from toxic compounds can cause injury to cells or prolonged stimulation. Changes in the nucleus of cells that experience necrosis are loss of chromatin, non-vescular wrinkled nuclei, picnotics, karyolysis and carioreksis [7]. Necrotic myocytes are myocardial cells that have signs of necrosis such as picnotics (shrinkage of the cell nucleus), cariorexis (destroyed cell nuclei) and karyolysis (cell nuclei disappear).

Emerging evidence supports the concept that hypertension may increase circulating pro-inflammatory mediators that induce oxidative stress. The NADPH oxidase controls the oxidative stress response which functions as an oxygen sensor to generate ROS from molecular oxygen. The upregulation of cardiac NOXs triggered by hypertension will trigger further inflammation [38]. Inflammation (inflammation) is the body's defense mechanism due to a tissue response to both local and internal destructive influences. The destructive effects (noxy) can be in the form of physical, chemical, bacterial, parasitic, acid, strong alkaline and bacteria [25].

In this case, the part of the heart that becomes the focal point of observation is the left ventricle. Research on the efficacy of herbal medicine as an antihypertensive against the heart has been carried out by [35], which stated that hypertension is an important factor in health worldwide, because it causes an increase in mortality and disability among people in many countries [28]. It is clear that hypertension is identified as a concomitant risk for cardiovascular disease. A well-known risk of cardiovascular-related death is left ventricular hypertrophy (LVH) [10].

The mechanisms that drive LVH to hypertension reveal a variety of key factors, including hemodynamic, endothelial, neuro-humoral and oxidative stress. Hypertension is characterized by an increase in arterial blood pressure (BP), and subsequently affects the structural and functional changes in the left heart ventricle. Chronic stress results in hypertrophic adaptation of the existing cardiomyocytes with an increase in width, followed by thickening of the left ventricular wall [18]. Thus, LVH is a sensitive indicator of early changes in the heart due to excessive stress in hypertension [13, 31]. In addition, it is an important risk factor for coronary heart disease, heart failure and stroke in hypertensive patients [18; 27]. Indeed, recent research has shown that LVH can increase heart-related mortality [23]. Therefore, increased cardiac performance can be achieved by inhibiting LVH independently of other risk factors [11].

It is known that hypertension is associated with ROS. The evidence provided suggests that redox-dependent pathways significantly contribute to the pathophysiology of hypertension [9] and high levels of ROS play a role in the pathophysiology of hypertensive cardiac remodeling [36]. The main feature of ROS-induced cellular injury is lipid peroxidation due to the effect of ROS on polyunsaturated fatty acids [16]. This results in disruption of the regulation of the lipid bilayer of the cell membrane and produces an unsaturated aldehyde, malondialdehyde (MDA) [16]. These metabolites are able to deactivate many cellular proteins by forming protein cross-links and causing cytotoxic effects [16]. Therefore, altering the bioavailability of ROS by reducing production and / or by increasing radical scavenging is a potential therapeutic modality for lowering blood pressure in hypertension and preventing left ventricular hypertrophy. Apart from enzymes that produce ROS, antioxidant defense systems are also important for dealing with oxidative stress. Hypertension intervention aims not only by increasing blood pressure, but also by reducing oxidative stress in individuals with high blood pressure which has been shown to be more effective in reducing the risk of cardiovascular disease [14].

4. Conclusion

Based on the results and discussion of the Histopathological Profile of the Heart in Hypertensive Rats (DOCA-Salt) Exposed to Benalu Mango Methanolic Extract (MMME) for 14, it can be concluded that the administration of mango parasite leaf methanolic extract (MMME) to male Wistar rats Rattus novergicus on exposure for 14 days with doses of 50 mg / KgBB, 100 mg / KgBB, and 200 mg / KgBB can reduce the number of heart cell necrosis in hypertensive rats (DOCA-Salt) and can reduce the diameter of heart organ cells (left ventricle) in hypertensive rats (DOCA-Salt).

Acknowledgment

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