THE EFFECT OF *MINDI* LEAF (*MELIA AZEDARACH* L.) FROM INDONESIA ON BLOOD PRESSURE IN WISTAR WHITE RATS (RATTUS NORVEGICUS) INDUCED BY DOCA-SALT (DEOXYCORTICOSTERONE ACETATE)

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ABSTRACT

Hypertension is a cardiovascular disease, one of world health problems. In the last decade hypertension disease prevalence tend to increase. *Mindi* Leaf (*Melia azedarach* L.) was used by Indonesian society to treat of hypertension.To analyze the effect of antihypertensive of ethanolic extract of Mindi Leaf (*Melia azedarach*) on rats mice Induced by DOCA-Salt (Deoxycorticosterone Acetate).This research type is true experimental laboratories with pretest-posttest control group design method. This study conducted on 30 male wistar rats induced by DOCA-Salt (Deoxycorticosterone acetate) 20mg / kgbw subcutaneously dissolved in corn oil for 7 days, given 2% NaC drink. Subjects divided into 6 groups, namely: H1 (positive controls made hypertensive and given Furosemide at a dose of 7.2mg / 200g.bw), H2 (negative control, hypertensive but not lowered), H3, H4, H5 were given extracts with respective concentrations (180 mg; 360mg; 720mg), H6 (normal group). Blood pressure measurement performed at day 0, day 8, and day-14.There was a difference in blood pressure before and after induction of Mindi Leaf (*Melia azedarach*) extract with p <0.05 in 180mg / 200gbw concentration on One Way Anova test and continued with Post Hoc LSD on negative control.*Mindi* Leaf (*Melia azedarach* L.) has antihypertensive effect and reaction rate is obtained at a concentration of 180mg / 200gbw.

Keyword: *Melia azedarach, Antihypertensive, flavonoid, Saponins, Kaempferol, Coumarin*

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INTRODUCTION

Cardiovascular disease is a major health problem in developed and developing countries, one of which is hypertension. Hypertension or high blood pressure is a condition where blood pressure increase over a long time, characterized by an increase in systolic pressure exceeding 140 mmHg and diastolic pressure exceeding 90 mmHg [1]. This condition can lead to increased morbidity rate (morbidity) and mortality rate (mortality) [2].Until now, hypertension is still a major problem in the world, both in developed and developing countries, including Indonesia [3] .Prevalence of hypertension in Indonesia is 30% with incidence of complications on cardiovascular disease by 52% for women more than in men by 48% (Health Department of Republic Indonesia, 2010). Hypertension is a multifactorial disease [4]. Factors responsible for the high incidence of hypertension are obesity, stress, genetic factors, old age, high salt intake and unhealthy lifestyles such as smoking, alcoholic drinking and lack of exercise [5].Management of hypertension performed non-medically by overcoming obesity, reducing salt intake, avoiding stress and improving unhealthy lifestyle and medically using drugs such as diuretics, Ca-channel blockers, β-blockers, ACE-inhibitors, vasodilators, and etc. Each drug has different side effects. [5,6].The use of drugs derived from natural products seen increasingly widespread today [7]. Accordance with the development and demands of the times, traditional medicine expected able to develop into a Fitofarmaka class of drugs which have an absolute requirement in term of quality assurance, efficacy and safety. Many people assume that the use of traditional drugs relatively safer than synthetic drugs but this does not mean that traditional drugs has no side effects or toxic effects [8-10].White Cedar leaf (Melia azeradach) used by Indonesians as traditional medicine [11]. This tree grows rapidly and originates from China [12]. This plant can grow as high as 10m - 20m, usually grown on the side of the road as a protective tree, sometimes also a part of wild trees near coastal area and could be found from lowlands to the highlands with an altitude of 1100 m above sea level [13].Azedarach used as an ayurveda medicine in India and medicines in Unani, in Arab countries as an antioxidant, analgesic, anti-inflammatory, rodent insecticide, anti-diarrheal, dectruksi, diuretic, antidiabetic, cathartic, emetic, antirheumatic and antihypertensive [14]. Ahmed, et al., (2012) says that compounds contained in the white cedar leaf are alkaloids, tannins, saponins, phenolic, penoid triter and flavonoids [15].The commonly used solvents for extracting the white cedar leaf are distilled water, ethanol, methanol, hexane, petroleum ether, ethyl acetate, and coroform [16]. This research used ethanol solvent, and maceration method. Maceration method is the process of extraction by soaking compounds using a particular solvent with occasionally shaken and stirred at room temperature, this process continues for several days until comparison of simplicia obtained with solvent as much as determined [17].Experimental and clinical studies prove that it has antioxidants, antimicrobials, anti-inflammatory, cardioprotective, analgesic, anticancer, antiulcer,

antipyretic, antiplasmodial and male contraceptive [18].This study aimed to analyze the antihypertensive effect and maximum concentration of white cedar leaf extract on antihypertensive activity in male wistar rats (Rattus norvegicus) made hypertensive.

MATERIAL AND METHODS

Research design

The type of research used was a true experimental laboratories, with the study design using a completely randomized design with pretest-posttest control group design.

Place and Time of research

This research conducted in Pharmacology Laboratory of Faculty of Pharmacy Universitas Gadjah Mada. Starting from April to June 2017.

Materials

white cedar Leaf Extract obtained from 3 Kg Leaves of white cedar (Melia adezarach) in Jetak, Sidoarjo, Sragen Regency. Which dried and extracted with 96% ethanol solvent by maceration method.

The extraction process starts from drying the fresh white cedar Leaf, then crushing with blender, sifting, then white cedar dried leaves powder dissolved in ethanol, distilled for 8 hours with acceleration spin 500 rpm with room temperature, then filtered and the filtrate taken, evaporated using evaporator with room temperature.

Animal Experiments

A total of 30 rats of wistar (*Rattus norvegicus*) rats weighing 100-200grams aged 2-3 months divided into 6 groups. A total of 30 rats sample randomly divided into 6 groups: H1 (Positive control, made hypertensive and given furosemide, furosemide dose 7,2 / 200gbw), H2 (negative control, made hypertensive and 25 ml / 200gbw NaCMC), H3, H4, H5 made hypertensive and then given white cedar daily extract for 7 days with dose 180 Mg / 200gbw, 360 mg / 200gbw, 720 mg/200gbw. Each group (except the normal Group) induced hypertension using DOCA-Salt 20mg / kgbw subcutaneously dissolved in corn oil for 7 days given 2% NaC drink. Then treated each group for the next 7 days.

Blood Pressure Measurement

All mice measured blood pressure on day 0, day 8, and day 14 used a CODATM Kent Scientific Corporation blood pressure gauge.

Data analysis

Blood Pressure data presented as the mean of each treatment group. Data analyzed using One Way Anova and continued with Post Hoc LSD.

RESULT AND DISCUSSION

Result

In the process of extraction of Mindi Leaf (*Melia azedarach*), we obtained 300 grams extract from 3 kg. The process of Mindi Leaf extract can be seen in Figures 1.2 and 3

Figure 1. Leaves of Mindi (Melia azedarach) that are distiller

Figure 2. Evaporation process Leaf Mindi (*Melia azedarach*)

Figure 3.Extract from Leaves of Mindi (*Melia azedarach*)

Measurement of blood pressure in wistar rats can be seen in figure 4.

Figure 4. Blood pressure measurement using CODA ^{TM} Kent Scientific Corporation

Blood pressure measurement held on days-0, day-8 and day-14. (table 1).

Table 1. Blood pressure measurement of rats on days-0, day-8 and day-14.

Group	**day-0 (**Before treatment**)**		**day-8** (after induction**)**		**day-14** (after induction**)**	
	sistole	**Diastole**	**sistole**	**diastole**	**Sistole**	**diastole**
Group 1	116	94	134	107	121	94
Group 2	131	106	147	107	129	93
Group 3	116	85	141	112	101*	71
Group 4	128	89	157	108	104*	75
Group 5	124	94	146	120	115	87
Group 6	113	82	126	93	114	84

Information :G1: Positive control;G2: Negative control;G3: Mindi Leaf Extract 180 gr / 200gbw;G4: Mindi Leaf Extract 360 gr / 200gbw;G5: Mindi Leaf Extract 720 gr / 200gbw;G6: Normal group*: Significant difference with negative control by LSD test (P<0.05).From analysis using One Way Anova p value is 0.032 (p <0.05) at systolic blood pressure on day 0, p value is 0.040 (p <0.05) for blood pressure on day 7, p value is 0.032 (P <0.24) for blood pressure on day 14.At blood pressure diastole value is 0.40 (p <0.05) for blood pressure on day 0, p value is 0.043 (p <0.05) for blood pressure on day 7, p value is 0.27 (p <0.05) for blood pressure on day. This shows that there is a difference in blood pressure after treated by *Mindi* Leaf extract in hypertensive rats

DISCUSSION

The result of research on Mindi Leaf (Melia azedarach) in white mice has anti-hypertension effect. There are so many reports that are available on the pharmaceutical potential of different types of biological activities of Melia azedarach L including diuretic activity, anti-hypertension, anti-inflammatory, antibacterial, antifungal, hepto-protection E, antioxidant, antitumor, anti-allergy and antimalarial [19.20].Chemical compound inside of mindi leaf has been known to play an active role in anti-hypertension mechanism including flavonoid, saponin, kaemferol, and coumarin. It is one of the largest phenols in nature. The compound can protect the body from free radical through antioxidant mechanism. Flavonoid is able to improve endothelial function and inhibit platelet aggregation. This effect is an advantage on the risk of cardiovascular disease [21].Flavonoid affects the work of *Angiotensin Converting Enzyme* (ACE). Inhibition of ACE will inhibit angiotensin I changes into angiotensin II, which causes vasodilation so that peripheral resistance resistance drops and can lower blood pressure. Other effects can lead to decreased retention of water and salt by the kidney, aldosterone secretion, and secretion of Anti Diuretic Hormone (ADH) by the hypopituitary gland. The decreased secretion of aldosterone affects the decreased retention of water and salt by the kidney, whereas decreased ADH secretion causes a decrease in water absorption. Decreased retention of water and salt and water absorption causes blood volume to decrease, resulting in decreased blood pressure [22].

Saponin has a diuretic property by declining plasma volume by excreting

water and electrolyte especially sodium, so in the end *cardiac output* decreases. Sodium and water can also affect peripheral resistance [23].

Alkaloid has the same function with β-blocker drugs that has negative inotropic and negative crono-tropic properties on the heart. The result is reduction of cardiac output, reduction of heartbeat and lack of contraction strength of the myocardium. Peripheral resistance sometimes increases, sometimes it is also constantly. Reduction of cardiac output that is chronic causing peripheral resistance declines. This causes a reduction of blood pressure [24].

After it is analyzed, *Mindi* Leaf extract (*Melia azedarach* L) has an anti-hypertension effect if it is compared to positive control and negative control. According to three groups of the extract treatment are given, with analysis Post Hoc LSD of extract groups with concentration 180mg/200gbw have anti-hypertension effect that are meant with value p< 0.16 in systolic pressure and p< 0.064 in diastolic pressure, it is compared to extract groups 360 mg/200gbw with value p< 0.378 in systolic pressure and p< 0.222 in diastolic pressure. Meanwhile, in concentration 720 mg/200gbw it already does not has anti-hypertension effect with value p>0,05 in systolic and diastolic pressure. It shows that the maximum concentration of *Mindi* leaf extract which has anti-hypertension effect is ± 360 mg/200gbw, or *Mindi* Leaf has anti-hypertension effect in low concentration.

Based on the data above, it is known that *Mindi* Leaf Extract (*Melia azedarach* L) is able to decline blood pressure in white rats wistar male induced hypertension with maximum concentration 180mg/200gbw.

CONCLUSION

Mindi Leaf Extract (*Melia azedarach* L.) has anti-hypertension effect with optimum concentration 180mg/200gbw.

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