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# UTILIZATION OF AFRICAN LEAVES (VERNONIA AMYGDALINA) TO LOWER BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION: A SYSTEMATIC REVIEW

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## ABSTRACT

**Introduction:** Hypertension is a non-communicable disease caused by genetics, stress, and lack of physical activity. So far, no effective drugs have been found to cure high blood pressure. Vernonia amygdalina contains substances that can lower blood pressure, namely flavonoids and potassium. **Purpose**: The systematic review aims to assess the potential of vernonia amygdalina in lowering blood pressure in hypertensive people. **Methods**: Articles are obtained from electronic databases such as PubMed, ScienceDirect, and Google Scholar published from 2011 to 2021. Keywords used: ("African leaf" OR "bitter leaf" OR "vernonia amygdalina") AND (hypertension OR "high blood pressure ") NOT" low blood pressure ". **Results**: The results of the six selected articles indicate that vernonia amygdalina is able to lower blood pressure. This is proved in the hypotensive experiments of cats, suggesting that vernonia amygdalina can affect a significant drop in blood pressure in normotensive cats. **Discussion**: The flavonoid content of vernonia amygdalina can increase the biogibility of nitrous oxide (NO) and cause vasodilatation and endothelium vasodilation. Potassium may also cause vasorrhea to react through a membrane hyperpolarizing and thus encourage the closing of the calcium channel. **Conclusion:** It can be determined that vernonia amygdalina's consumption potentially lowers blood pressure in hypertensive people.

**Keywords:** hypertension, blood pressure, Vernonia amygdalina

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## INTRODUCTION

Hypertension is a non-communicable disease (PTM) that is characterized by systolic blood pressure that rises to 140 mmHg and diastolic blood pressure that reaches 90 mmHg in repeated measurements (Yonata, A. et al., 2016). Hypertension is included in the silent disease. This is because the patient will only know that he has hypertension after checking his blood pressure and because this disease does not have distinctive symptoms (Agrina, A. et al., 2011). This disease must be handled appropriately because if there is an error of control and treatment, it can cause complications such as a stroke. Hypertension is a degenerative disease, so to minimize the risks that occur (Astuti, A., 2016). Herbal medicine is an alternative in the treatment of hypertension sufferers, one of which is by using vernonia amygdalina or in Indonesian it is called African leaves. The side effects of herbal medicines are believed to be fewer than chemical drugs.

Vernonia amygdalina contains many chemical and nutritional compounds. The nutrients contained are 4.7% fat, 68.4% carbohydrates, 19.2% fiber, 19.2% protein, 30 mg / 100g carotenoids, 166.5 mg / 100g ascorbic acid, 7.5 mg / 100 iron. grams, and calcium 0.97g / 100g(Sukmawati et al., 2017). Bioactive compounds that have been identified from vernonia amygdalina include flavonoids, saponins, alkaloids, tannins, phenolics, terpenes, steroid glycosides, triterpenoids, and lactone sesquiterpenes. These bioactive compounds cause vernonia amygdalina to have various pharmacological

activities that are beneficial to its use as a treatment candidate. herbs. Vernonia amygdalina contains flavonoids which can be extracted from the leaves using organic solvents. Flavonoids are a group of naturally occurring bioactive compounds found in plants and are a group of phenolic compounds. The pharmacological activity of flavonoids has been widely studied as antioxidants (Bestari, R., 2021).

The content of flavonoids as antioxidants can increase the bioavailability of nitric oxide (NO) by trapping superoxide in the body (Musyayyadah, SA et al., 2019). This causes vasodilation and endolytium vasorelaxation to decrease blood pressure in the body. Therefore, research is needed to determine the potential of vernonia amygdalina as an antihypertensive. This systematic review aims to evaluate the use of vernonia amygdalina for lowering blood pressure.

## METHOD

This study uses a systematic review method. The steps in this study are summarized in Figure 1. Articles were obtained from electronic databases published in PubMed, Science Direct, and Google Scholar, published from 2011 to 2021. Search for articles using a keyword structure:("african leaf" OR "bitter leaf" OR "Vernonia Amygdalina") AND (hypertension OR "high blood pressure") NOT "low blood pressure". The criteria for the articles used in the study were articles that were limited in the last ten years, in English, available in full text, and containing the use of vernonia amygdalina to lower blood pressure.

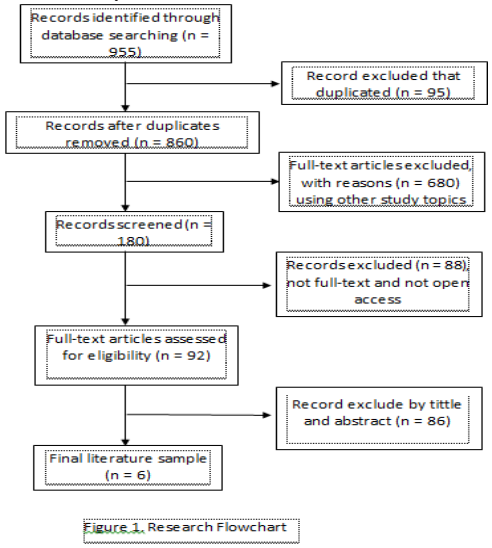


Figure 1. Research Flowchart

The number of articles obtained from the PubMed 3, Science Direct 90, and Google Scholar databases was 862. Articles that were double-published by PubMed, Science Direct, and Google Scholar were selected, and 860 were left. Furthermore, a review was carried out by eliminating articles that used other study topics, so that 180 articles were obtained. The review was carried out again by issuing 88 articles that were not available in full-text pdf form, and after this review, 92 articles were obtained. Then the articles were reviewed by looking at the title and abstract of each article to see indicator variables that showed the use of vernonia amygdalina to lower blood pressure, so there were 6 articles that met the inclusion criteria.

## RESULT

Comparison of African Leaf Content (Vernonia amygdalina Del.)

A study shows that vernonia amygdalina contains many chemical and nutritional compounds. Vernonia amygdalina contains chemical compounds including flavonoids, saponins, coumarin, xanton, lignans, phenolic acids, peptides, terpenes, and luteolin. While the nutrients contained in vernonia amygdalina, namely 4.7% fat, 68.4% carbohydrates, 19.2% fiber, 19.2% protein, carotenoids 30 mg / 100g, ascorbic acid 166.5 mg / 100g, iron 7.5 mg / 100 grams, calcium 0.97g / 100g, potassiumphosphorus, sulfur, manganese, sodium, zinc, copper, selenium and magnesium. The main benefits of vernonia amygdalina are as a medicine for hypertension, diabetes, gout, and cancer(Ijeh, II et al., 2011).

The decrease in blood pressure of African leaves is mediated through vasorelaxation. The results showed that the greatest vasorelaxant activity was shown by the ethanol extract of vernonia amygdalina (VAE). The vasorelaxant activity of VAE depends on the percentage of ethanol used. Vasorelaxant activity was shown by ethanol extract 95%. The 95% ethanol extract only needed a low dose to reduce the precontracted aortic ring, with an EC50 value of 6.78 ± 0.66 mg / mL. The 50% ethanol extract also showed vasorelaxant properties, but it was not as good as the 95% ethanol extract with an EC50 value of 11.41 ± 1.50 mg / mL(Ch'ng, YS et al., 2016).

African Leaf Mechanism of Action (Vernonia amygdalina Del.) as an antihypertensive Blood vessels can adapt to changing parameters including temperature, nerve signals, and mechanical strength. Blood vessels isolated from living organisms can be used as research

materials in vitro studies on antihypertensive drug research (Yildiz, O. et al., 2013). Blood pressure that is regulated in a narrow range will not cause damage to the vascular system, especially to the endothelium and smooth muscle cells (Loh et al., 2016). The endothelium and smooth muscle cells tightly regulate the resistance of the vascular system through stimulation of internal or external vasoactive compounds that act on channels, receptors, or enzymes in blood vessels (Joshua, ZP et al., 2012). VAE shows vasorelaxation of the intact endothelium of the aortic ring. The effect of this vasorelaxant decreases significantly but still ends up with a high vasorelaxant effect. This suggests that the vasorelaxant effect mediated by VAE is not only endothelial dependent but also partly influenced by endothelial independent relaxant factors.(Ch'ng, YS et al., 2017).

Vascular resistance is also regulated by membrane potential which is generally regulated through the correlation between different ion channels, including potassium and calcium channels. There are four types of potassium channels used, namely KCa, Kir, KATP, and Kv tested using their respective antagonists. The function of the potassium channels in regulating the electrochemical gradient in the cell is to control the action potential. Activation of the potassium channels can cause membrane hyperpolarization which promotes the closure of calcium channels and causes vasorelaxation(Yildiz, O. et al., 2013).

The movement of calcium ions also plays a role in the regulation of vascular resistance through action potency. Activation of voltage operated calcium channels (VOCC) causes the entry of extracellular calcium ions into the cytosol, which occurs with an increase in extracellular potassium conductance and depolarization of the vascular smooth muscle cells (VSMC) membrane. Relatively speaking, concentration ethylene glycol-bis (β-aminoethyl ether) -N, N, N ′, N′-tetraacetic acid (Low EGTA) is used to deplete calcium from isolated aortic rings prior to antagonist pretreatment and incubation with calcium buffer. The addition of calcium chloride in cumulative concentrations was successful in eliciting a concentration- dependent vasoconstriction response in the control, positive, and experimental sets. Significant inhibition of VAE in the contractile response induced by extracellular calcium ingress suggests a vasorelaxant effect from extracts administered across isolated aortic rings is abundantly mediated by VOCC. VAE can reduce concentration-dependent vasoconstriction of PE by inhibiting the intracellular release of calcium into the cytosol via IP3 receptors (Ch'ng, YS et al., 2017).

## DISCUSSION

High blood pressure (hypertension) is a disease that is quite dangerous in the world. Hypertension itself can trigger cardiovascular diseases such as heart failure, stroke, heart attack, and kidney failure (Siswanto, Y. et al., 2020). Factors that cause hypertension include genetic factors, obesity, increased stress, lack of physical activity, smoking habits, age, and high consumption of salty foods, caffeine, and MSG (monosodium glutamate). Foods that contain lots of sodium can trigger hypertension. This is because when sodium is absorbed into the blood vessels, it will cause water retention and an increase in blood volume (Purwono, J. et al., 2020)

In ethnobotany studies, it is stated that the relationship between humans and plants is very close. Where plants will always be used by humans in life, one of which is the use of extraction of active substances found in plants(Abiulo, O., 2018). Vernonia amygdalina is a small tree or shrub measuring 2-5 meters, petiolate leaves with a diameter of 6 mm, elliptical in shape, green leaves, distinctive aroma, and a bitter taste so it is called bitter leaf (Adeniyi, SA et al., 2012). African leaf or bitter leaf or vernonia amygdalina is a plant that is associated with therapeutic or diagnostic agents in managing disease. This vernonia amygdalina has a high iron content, where iron is the main component of hemoglobin carryingO_2 (oxygen) from red blood cells (Joshua, ZP et al., 2012).

In a study, states that vernonia amygdalina contains bioactive constituents such as alkaloids (1.90 mg / 100 gr), tannins (0.07 mg / 100 gr), saponins (2.94 mg / 100 gr), flavonoids (2, 98 mg / 100 gr), phenol (0.07 mg / 100 gr), ascorbic acid or vitamin C (310.62 mg / 100 gr), niacin (0.80 mg / 100 gr), riboflavin (0.09 mg / 100 gr), thiamine (0.08 mg / 100 gr), and is a good source of minerals, it can be in the form of macro minerals such as potassium (5.86 mg / 100 gr) and calcium (0.97 mg / 100 gr) and in the form of micro minerals such as iron (2.73 mg / 100 gr) and zinc (0.51 mg / 100 gr) (Adeniyi, SA et al., 2012).The mineral content of potassium and flavonoids in vernonia amygdalina has a fairly high number. Where the two compounds can be useful for lowering diastolic and systolic blood

pressure. This is because consuming potassium can increase the concentration of intracellular fluid, so it tends to increase the concentration in the extracellular and lower blood pressure (Atun, L. et al., 2014). The content of flavonoids as antioxidants can increase the bioavaibility of nitric oxide (NO) through trapping superoxide in the body which causes vasodilation and endolytium vasorelaxation so that blood pressure in the body decreases (Musyayyadah, SA et al., 2019).

Other compounds present in vernonia amygdalina are 4.7% fat, 68.4% carbohydrates, 19.2% fiber, 19.2% protein, 30 mg / 100g carotenoids, 166.5 mg / 100g ascorbic acid, 7 iron, 5 mg / 100 grams, calcium 0.97g / 100g, steroid glycosides that cause a bitter taste and also sesquiterpene compounds (vernodalin and vernomygdin) (Siswanto, Y. et al, 2020, Hasan, IC et al 2018). Of the many compounds in vernonia amygdalina, this plant has many benefits for treating various diseases, including hypertension (high blood pressure), diabetes, colorectal cancer, stomach disorders, skin blemishes, typhoid fever, malaria fever, excess body weight, constipation, and so forth(Abiolu, O., 2018, Hasan, IC et al 2018, Joshua, ZP et al., 2012). A study on the hypotensive effect states that vernonia amygdalina functions in reducing blood pressure in normotensive cats significantly so that vernonia amygdalina extract can be used to manage blood pressure in people with hypertension (Buraimoh, AA et al. 2014).

## CONCLUSION

Based on the systematic review that has been made, it can be concluded that African leaves (Vernonia amygdalina) can lower blood pressure through the content of flavonoids which can increase the bioavaibility of nitric oxide (NO), and potassium can cause vasorelaxation through hyperpolarization of the membrane, thereby lowering blood pressure.

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Table 1. Utilization of African Leaves (Vernonia amygdalina) to Lower Blood Pressure

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|---|---|---|
| **Result** | Atropine tends to have a stronger blocking effect on acetylcholine than leaf extract. | Low dose (5 mg/kg): dose-dependent bi-phasic systolic and diastolic blood pressure changes. Dose 10 mg / kg: transient mean arterial pressure increase of 73.7 + 3.4 mmHg. to 101.9 + 4.1 mmHg. |
| **Indicator Variables** | Atropine, acetylcholine, v*ernonia amygdalina* leaf extract. | Changes in systolic bi-phasic, diastolic blood pressure, and mean arterial pressure. |
| **Intervention** | The nomotic cat was sedated with sodium thiopentane intraperitoneally, then injected using aqueous leaf extract of v*ernonia amygdalina* at different doses, namely 1 mg/ml, 10 mg/ml, and 100 mg/ml into the femoral artery. After that, heparin is injected as a coagulant to prevent blood clots. Then, continued with the administration of atropine and acetylcholine. | 1. The mice were sedated with 25% urethane & 1% chloralose by intraperitoneal injection. Trachea, artery, and femoral vein open gently dissected & cannulated immediately to improve ventilation.<br>2. The rats were sacrificed with cervical dislocation, the thoracic aorta was removed, freed from the connective tissue, cut a 2 mm ring segment, and place in a stained dish filled with saline physiological solution. |
| **Design / Sample** | Experiment with animals.<br>Sample: nomotic cats. | Performed in vitro experiments on the isolated animal aorta.<br>Sample: Sprague-Dawley rats weighing 200 - 250 gr. |
| **Destination** | To evaluate the hypotensive effect of *vernonia amygdalina* leaf extract against nomotic cats. | To examine the effects of administering *vernonia amygdalina* on blood pressure, heart rate, and contractile response |
| **Reference** | 7 | 17 |