

ANTIHYPERTENSIVE EFFECTS OF SOME MEDICINAL PLANTS IN INDONESIA: A
REVIEW

Lia Eka Budiyanti, Monica Yashna Kusuma Adi Saputra, Samsi Ayu Wulandari, Sulastri Amallia, Ayu Jasmine Azzahra, Bela Cindika Sagala, Agnes Dewi Maria, Shintya Happy Herawati, Eka Nurfarida Musfiroh, Syifa Salsabila Nur Fauziah, Fadia Ainun Sathi'ah, Azzahra Amelia, Syifa Kamilah, Seftiani Su'aida Mahfud and Maulana Yusuf Alkandahri*

Faculty of Pharmacy, Universitas Buana Perjuangan Karawang, Karawang, West Java, Indonesia.



*Corresponding Author: Maulana Yusuf Alkandahri

Faculty of Pharmacy, Universitas Buana Perjuangan Karawang, Karawang, West Java, Indonesia.

Article Received on 04/01/2024

Article Revised on 25/01/2024

Article Accepted on 15/02/2024

ABSTRACT

Regarding the use of herbal medicines to treat hypertension (cardiovascular disease), efficacy and safety are of the utmost importance. At present, scholars are commencing the search for novel antihypertensive compound candidates derived from naturally occurring substances that have demonstrated antihypertensive effects through empirical evidence. Scholars are conducting this search as an alternative to the currently problematic antihypertensive drugs. Scientific validation has confirmed that several indigenous Indonesian medicinal plants, including *Apium graveolens*, *Centella asiatica*, *Annona muricata*, *Allium sativum*, *Imperata cylindrica*, *Ocimum basilicum*, and *Persea americana*, possess antihypertensive properties through distinct mechanisms. Consequently, the potential antihypertensive effects of some medicinal plants in Indonesia are investigated in this review article.

KEYWORDS: Antihypertensive, Medicinal plants, *Apium graveolens*, *Centella asiatica*, *Annona muricata*, *Allium sativum*, *Imperata cylindrica*, *Ocimum basilicum*, *Persea americana*.

INTRODUCTION

The diagnostic criteria for hypertension, also known as high blood pressure, are systolic and diastolic blood pressures exceeding 140 mmHg and 90 mmHg, respectively. Due to the fact that hypertension is a major risk factor for coronary artery disease and its complications, including heart failure, stroke, kidney disease, and diabetes, this condition is among the leading causes of death on a global scale.^[1] The World Health Organization projects that by 2025, hypertension will affect 1.5 billion individuals and be the cause of over 7 million annual deaths.^[2] At present, a multitude of antihypertensive medications are available, including beta blockers, angiotensin-converting enzyme (ACE) inhibitors, and calcium channel blockers. However, this antihypertensive drug, extensively prescribed for the management of hypertension and cardiovascular disease, is also associated with undesirable side effects.^[3,4] Angiotensin receptor blockers, ACE inhibitors, and calcium channel blockers can cause swelling in the face, lips, and throat in both kids and adults.^[5] Kumbhare et al., and Jung et al., have documented additional adverse effects of antihypertensive medications, such as facial flushing, shortness of breath, cough, hair loss, and headache.^[2,6] Therefore, because of their natural composition and use of medicinal plants, herbal

medicines and other alternative therapies are preferred.^[7,8] Currently, researchers are focusing on discovering novel antihypertensive medications derived from natural sources. Researchers are investigating active compounds found in botanical medicines historically used in different regions of Indonesia to treat hypertension.^[9-11] The objective is to identify novel antihypertensive compounds characterized by minimal toxicity and mild side effects so as to prevent patient harm.^[12,13] Consequently, the potential antihypertensive effects of some medicinal plants in Indonesia are investigated in this review article.

Apium graveolens

Apium graveolens is defined as a plant belonging to *Apiaceae* family, as a constituent in traditional medicine since ancient times, people across multiple nations have used this plant. Every component of this plant finds extensive application in culinary preparations, including salads and soups. *A. graveolens* has been attributed with several pharmacological properties, including anticancer, antiobesity, antihepatotoxic, and antihypertensive effects.^[14] Moghadam et al., demonstrated that administering *A. graveolens* extract intraperitoneally at a dose of 300 mg/kg could significantly reduce blood pressure in hypertensive mice induced by

deoxycorticosterone acetate.^[15] Also, a randomized, triple-blind, placebo-controlled, cross-over clinical trial showed that giving patients 1.34 g/day of *A. graveolens* seed extract for four weeks lowered their blood pressure significantly and brought it back to normal levels.^[16]

Centella asiatica

Centella asiatica is defined as a plant belonging to *Apiaceae* family as a traditional remedy in multiple countries, Indonesia being among them. Researchers believe that the broad-ranging therapeutic properties of *C. asiatica*, including the treatment of amenorrhea, genitourinary tract diseases in women, leprosy, lupus, varicose ulcers, eczema, psoriasis, diarrhea, fever, and anxiety relief, can be attributed to its primary constituents, triterpenoids and saponins.^[17] Bunaim *et al.*, found that mice with chronic high blood pressure caused by N(G)-nitro-L-arginine methyl (L-NAME) could have a big drop in blood pressure when they were given 500 mg/kg of *C. asiatica* extract by mouth. *C. asiatica* replenishes nitric oxide (NO) levels, which are reduced due to L-NAME induction, thereby attributing to its antihypertensive effect. Furthermore, *C. asiatica* impedes the elevation of angiotensin-converting enzyme (ACE) activity in the cardiac muscle induced by L-NAME.^[18]

Annona muricata

Annona muricata with its oval, dark green leaves and spiny green, white-fleshed fruit distinguish a tropical plant. Balderrama-Carmona *et al.*, reported frequent utilization of the fruit of this plant in the preparation of juice, ice cream, and as a food additive.^[19] *A. muricata* plant is believed to aid in the treatment of cancer, gout, tumors, hypertension, diabetes mellitus, ulcers, diarrhea, and allergies.^[20] According to the report, chronic hypertensive mice induced by ethanol and sucrose solution experienced a substantial reduction in blood pressure through cardiac output and/or total peripheral resistance, leading to a decrease in blood volume, when administered *A. muricata* orally at doses of 50, 100, and 150 mg/kg. Increased blood flow into peripheral blood vessels ultimately decreases the pressure on the blood vessel walls.^[21,22]

Allium sativum

Garlic, scientifically known as *Allium sativum*, is a root vegetable renowned for its piquant flavor and extensive global application as a seasoning and spice. The primary contributors to the spicy effect and aroma are organosulfur compounds, including allicin and diallyl disulfide.^[23] Historically, garlic has been recognized for its diverse array of biological activities, including anticarcinogenic, antioxidant, antidiabetic, renoprotective, anti-atherosclerotic, antibacterial, antifungal, and antihypertensive properties.^[24-26] Furthermore, garlic possesses antipyretic, sedative, and diuretic properties and has been utilized in traditional medicine to treat infections of the respiratory and urinary tracts, the cardiovascular system, and digestive

disorders.^[27] According to clinical trials, people with essential hypertension who took 300, 600, 900, 1200, or 1500 mg of *A. sativum* every day saw a big drop in their systolic and diastolic blood pressure over the course of 24 weeks.^[28] Garlic reduces blood pressure through the modulation of various mechanisms, such as the renin-angiotensin system, renal tubular transport mechanisms, and prostaglandin system.^[29] According to Al-Qattan *et al.*, garlic also lowers blood pressure by making the direct and indirect vasodilator effects of NO stronger. This happens by increasing the production of NO.^[29]

Imperata cylindrica

Imperata cylindrica is defined as a medicinal plant from the *Gramineae* family that is known to have 72 chemical constituents that have been isolated and identified, among which saponins, flavonoids, phenols, and glycosides are the main constituents. This plant is known to have various pharmacological activities, including hemostasis, repair of the urinary tract, anti-inflammatory, antibacterial, anti-cancer, and improving the immune system.^[30] Oral administration of *I. cylindrica* at doses of 60, 90, and 115 mg/kg for 14 days to hypertensive mice induced by NaCl solution was reported to reduce blood pressure significantly by reducing heart rate.^[31]

Ocimum basilicum

Ocimum basilicum is defined as a species in the *Lamiaceae* family known for having various medicinal properties.^[32] Traditionally, people use this plant as an antimalarial, antirheumatic, anticholesterol, antihypertensive, painkiller, and for the treatment of stroke.^[33,34] Qamar *et al.*, and Umar *et al.*, reported that administering *O. basilicum* orally to hypertensive mice induced by L-NAME at a dose of 50 mg/kg for 28 days significantly reduced systolic and diastolic blood pressure by inhibiting endothelin and angiotensin-II.^[35,36]

Persea americana

Persea americana is defined as a plant belonging to the *Lauraceae* family that is commonly used as an ingredient in traditional medicine in several countries. Traditional medicine uses this plant to treat various diseases, including menorrhagia, hypertension, stomachache, bronchitis, diarrhea, and diabetes.^[37] Oral administration of *P. americana* at doses of 50, 100, and 150 mg/kg to hypertensive mice induced by ethanol and sucrose solution was reported to reduce systolic and diastolic blood pressure significantly by reducing cardiac output and/or total peripheral resistance, thus causing a decrease in the total volume of blood flowing into peripheral blood vessels, which ultimately reduces the pressure on the blood vessel walls.^[21,22]

CONCLUSION

Scientific studies have empirically proven the blood pressure-lowering effects of all these plants. This cannot be separated from the active compounds contained in these plants, which have antihypertensive properties with different mechanisms of action. Research on medicinal

plants can improve antihypertensive treatment. However, further research must be carried out to determine the effectiveness of these plants as antihypertensives so they can be used in the latest treatment of hypertension.

REFERENCES

1. Abegaz TM, Shehab A, Gebreyohannes EA, Bhagavathula AS, Elnour AA. Nonadherence to antihypertensive drugs: A systematic review and meta-analysis. *Medicine (Baltimore)*, 2017; 96(4): 1-9.
2. Jung IH, Kim SE, Lee YG, Kim DH, Kim H, Kim GS, *et al.* Antihypertensive effect of ethanolic extract from *Acanthopanax sessiliflorus* fruits and quality control of active compounds. *Oxid Med Cell Longev*, 2018; 2018: 1-14.
3. Pal SK, Shukla Y. Herbal medicine: current status and the future. *Asian Pac J Cancer Prev.*, 2003; 4(4): 281-288.
4. Niaz T, Hafeez Z, Imran M. Prospectives of Antihypertensive Nano-ceuticals as Alternative Therapeutics. *Curr Drug Targets*, 2017; 18(11): 1269-1280.
5. Shapovalov G, Skryma R, Prevarskaya N. Calcium channels and prostate cancer. *Recent Pat Anticancer Drug Discov*, 2013; 8(1): 18-26.
6. Kumbhare RM, Kosurkar UB, Bagul PK, Kanwal A, Appalanaidu K, Dadmal TL, *et al.* Synthesis and evaluation of novel triazoles and mannich bases functionalized 1,4-dihydropyridine as angiotensin converting enzyme (ACE) inhibitors. *Bioorg Med Chem.*, 2014; 22(21): 5824-5830.
7. Alkandahri MY, Berbudi A, Subarnas A. Active compounds and antimalaria properties of some medicinal plants in indonesia – A review. *Sys Rev Pharm.*, 2018; 9(1): 64-69.
8. Alkandahri MY, Maulana YE, Subarnas A, Kwarteng A, Berbudi A. Antimalarial activity of extract and fractions of *Cayratia trifolia* (L.) Domin. *Int J Pharm Res.*, 2020; 12(1): 1435-1441.
9. Alkandahri MY, Sujana D, Hasyim DM, Shafirany MZ, Sulastri L, Arfania M, *et al.* Antidiabetic activity of extract and fractions of *Castanopsis costata* leaves on alloxan-induced diabetic mice. *Pharmacogn J.*, 2021; 13(6): 1589-1593.
10. Alkandahri MY, Kusumiyati K, Renggana H, Arfania M, Frianto D, Wahyuningsih ES, *et al.* Antihyperlipidemic activity of extract and fractions of *Castanopsis costata* leaves on rats fed with high cholesterol diet. *RASĀYAN J Chem.*, 2022; 15(4): 2350-2358.
11. Nuraeni E, Alkandahri MY, Tanuwidjaja SM, Fadhilah KN, Kurnia GS, Indah D, *et al.* Ethnopharmacological study of medicinal plants in the Rawamerta Region Karawang, West Java, Indonesia. *Open Access Maced J Med Sci.*, 2022; 10(A): 1560-1564.
12. Alkandahri MY, Berbudi A, Utami NV, Subarnas A. Antimalarial Activity of Extract and Fractions of *Castanopsis costata* (Blume) A.DC. *Avicenna J Phytomed*, 2019; 9(5): 474-481.
13. Alkandahri MY, Yuniarsih N, Berbudi A, Subarnas A. Antimalaria activities of several active compounds from medicinal plants. *Pharmacogn J.*, 2022; 14(1): 245-252.
14. Abody MSA. Cytotoxic, antioxidant, and antimicrobial activities of Celery (*Apium graveolens* L.). *Bioinformation*, 2021; 17(1): 147-156.
15. Moghadam MH, Imenshahidi M, Mohajeri SA. Antihypertensive effect of celery seed on rat blood pressure in chronic administration. *J Med Food.*, 2013; 16(6): 558-563.
16. Rad MS, Moohebaty M, Mohajeri SA. Effect of celery (*Apium graveolens*) seed extract on hypertension: A randomized, triple-blind, placebo-controlled, cross-over, clinical trial. *Phytother Res.*, 2022; 36(7): 2889-2907.
17. Gohil KJ, Patel JA, Gajjar AK. Pharmacological review on *Centella asiatica*: A potential herbal cure-all. *Indian J Pharm Sci.*, 2010; 72(5): 546-556.
18. Bunaim MK, Kamisah Y, Mohd Mustazil MN, Fadhilullah Zuhair JS, Juliana AH, Muhammad N. *Centella asiatica* (L.) Urb. prevents hypertension and protects the heart in chronic nitric oxide deficiency rat model. *Front Pharmacol*, 2021; 12: 1-12.
19. Balderrama-Carmona AP, Silva-Beltrán NP, Gálvez-Ruiz JC, Ruíz-Cruz S, Chaidez-Quiroz C, Morán-Palacio EF. Antiviral, antioxidant, and antihemolytic effect of *Annona muricata* L. leaves extracts. *Plants (Basel)*, 2020; 9(12): 1-11.
20. Mutakin M, Fauziati R, Fadhilah FN, Zuhrotun A, Amalia R, Hadisaputri YE. Pharmacological activities of soursop (*Annona muricata* Lin.). *Molecules*, 2022; 27(4): 1-17.
21. Sokpe A, Mensah MLK, Koffuor GA, Thomford KP, Arthur R, Jibira Y, *et al.* Hypotensive and Antihypertensive Properties and Safety for Use of *Annona muricata* and *Persea americana* and Their Combination Products. *Evid Based Complement Alternat Med.*, 2020; 2020: 1-13.
22. Siddiqui A. Effects of vasodilation and arterial resistance on cardiac output. *J Clinic Experiment Cardiol*, 2010; 2(11): 1-6.
23. Tesfaye A, Mengesha W. Traditional uses, phytochemistry and pharmacological properties of garlic (*Allium sativum*) and its biological active compounds. *Int J Sci Res Eng Technol.*, 2015; 1: 142-148.
24. Rahman K, Lowe GM. Garlic and cardiovascular disease: a critical review. *J. Nutr.*, 2006; 136(3): 736S-740S.
25. Davis SR. An overview of the antifungal properties of allicin and its breakdown products--the possibility of a safe and effective antifungal prophylactic. *Mycoses*, 2005; 48(2): 95-100.
26. Badal DS, Dwivedi AK, Kumar V, Singh S, Prakash A, Verma S, *et al.* Effect of organic manures and inorganic fertilizers on growth, yield and its

- attributing traits in garlic (*Allium sativum* L.) *J Pharmacogn Phytochem*, 2019; 8: 587-590.
27. Souza GA, Ebaid GX, Seiva FR, Rocha KH, Galhardi CM, Mani F, *et al.* N-acetylcysteine an allium plant compound improves high-sucrose diet-induced obesity and related effects. *Evid Based Complement Alternat Med.*, 2011; 2011: 1-7.
 28. Ashraf R, Khan RA, Ashraf I, Qureshi AA. Effects of *Allium sativum* (garlic) on systolic and diastolic blood pressure in patients with essential hypertension. *Pak J Pharm Sci.*, 2013; 26(5): 859-863.
 29. Al-Qattan KK, Khan I, Alnaqeeb MA, Ali M. Thromboxane-B2, prostaglandin-E2 and hypertension in the rat 2-kidney 1-clip model: A possible mechanism of the garlic induced hypotension. *Prostaglandins Leukot Essent Fatty Acids*, 2001; 64(1): 5-10.
 30. Jung YK, Shin D. *Imperata cylindrica*: A review of phytochemistry, pharmacology, and industrial applications. *Molecules*, 2021; 26(5): 1-13.
 31. Ruslin, Asmawi MZ, Rianse U, Sahidin I, Dhianawaty D, Soemardji AA, *et al.* Anti-hypertensive activity of alang-alang (*Imperata cylindrica* (L.) Beauv. root methanolic extract on male wistar rat. *Int J Res Pharm Sci.*, 2013; 4(4): 537-542.
 32. Karpiński TM. Essential oils of *Lamiaceae* family plants as antifungals. *Biomolecules*, 2020; 10(1): 1-35.
 33. Taek MM, Bambang PEW, Agil M. Plants used in traditional medicine for treatment of malaria by Tetun Ethnic people in West Timor Indonesia. *Asian Pac J Trop Med.*, 2018; 11: 630-637.
 34. Silalahi M, Nisyawati, Walujo EB, Supriatna J, Mangunwardoyo W. The local knowledge of medicinal plants trader and diversity of medicinal plants in the Kabanjahe Traditional Market, North Sumatra, Indonesia. *J. Ethnopharmacol*, 2015; 175: 432-443.
 35. Qamar F, Sana A, Naveed S, Faizi S. Phytochemical characterization, antioxidant activity and antihypertensive evaluation of *Ocimum basilicum* L. in l-NAME induced hypertensive rats and its correlation analysis. *Heliyon*, 2023; 9(4): 1-20.
 36. Umar A, Imam G, Yimin W, Kerim P, Tohti I, Berké B, *et al.* Antihypertensive effects of *Ocimum basilicum* L. (OBL) on blood pressure in renovascular hypertensive rats. *Hypertens Res.*, 2010; 33(7): 727-730.
 37. Yasir M, Das S, Kharya MD. The phytochemical and pharmacological profile of *Persea americana* Mill. *Pharmacogn Rev.*, 2010; 4(7): 77-84.