

SELECTED INDONESIAN MEDICINAL PLANTS FOR THE MANAGEMENT OF  
CARDIOVASCULAR DISEASE – A REVIEW

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Article Received on 12/03/2024

Article Revised on 02/04/2024

Article Accepted on 22/04/2024

**ABSTRACT**

An increase in the production of free radicals or the formation of toxic reactive oxygen species (ROS), including hydroxyl radicals, hydrogen peroxide, and superoxide radicals, causes oxidative stress. This stress is a significant contributor to cardiovascular diseases, including atherosclerosis, congestive heart failure, arrhythmia, and ischemic heart disease. At present, scientists are commencing the search for novel candidates for cardioprotective compounds derived from naturally occurring substances that have been empirically demonstrated to possess cardioprotective properties. Scientists are replacing cardiovascular medications, which currently display numerous hazardous adverse effects, with these novel candidates. Scientists have demonstrated the cardioprotective properties of medicinal plants indigenous to Indonesia, such as *Orthosiphon stamineus*, *Moringa oleifera*, *Punica granatum*, *Sonchus arvensis*, *Centella asiatica*, *Morinda citrifolia*, and *Averrhoa bilimbi*, via distinct mechanisms. Therefore, this review article is aimed to describe the potential cardioprotective properties of several indigenous Indonesian medicinal plants.

**KEYWORDS:** Cardioprotective, *Orthosiphon stamineus*, *Moringa oleifera*, *Punica granatum*, *Sonchus arvensis*, *Centella asiatica*, *Morinda citrifolia*, *Averrhoa bilimbi*.

**INTRODUCTION**

The escalation in prevalence rates of cardiovascular disease over the past two decades has rendered it a significant worldwide concern.<sup>[1-3]</sup> 31% of the world's population, or approximately 17.9 million individuals, succumb to cardiovascular disease annually. Where access to treatment is limited, developing countries account for over 75% of cardiovascular disease-related fatalities.<sup>[4]</sup> Four out of every five deaths attributed to cardiovascular disease are caused by strokes and heart attacks.<sup>[5]</sup> Existing pharmaceuticals, too, are accompanied by various adverse effects and a lack of effectiveness.<sup>[6]</sup> A variety of drug classes and combination drugs are commercially accessible for the purpose of managing cardiovascular disease.<sup>[7]</sup> Nevertheless, the overall course of treatment is quite costly and can result in severe to fatal side effects.<sup>[8]</sup> Hence, the exploration of novel potential cardioprotective compounds, including those derived from natural constituents, is imperative.<sup>[9,10]</sup>

Indonesia ranks second globally in terms of forest biodiversity, encompassing 2,500 medicinal plant species out of a total of 28,000.<sup>[11-13]</sup> Presently, ongoing research endeavors are focused on discovering novel

cardioprotective compounds derived from natural sources. One such approach involves investigating active compounds present in medicinal plants, which have historically been utilized across different regions of Indonesia to treat a variety of cardiovascular ailments.<sup>[14-16]</sup> The objective is to identify novel cardioprotective compounds characterized by minimal toxicity and mild side effects so as to prevent patient harm.<sup>[17-19]</sup> Therefore, this review article is aimed to describe the potential cardioprotective properties of several indigenous Indonesian medicinal plants.

***Orthosiphon stamineus***

*Orthosiphon stamineus* is a traditional medicinal plant which has various properties in treating various diseases, including kidney nephritis, cancer and arthritis. This plant is reported to contain bioactive pentacyclic compounds of triterpenes, betulinic acid, oleanolic acid, ursolic acid,  $\beta$ -sitosterol, and more than 20 other phenolic compounds.<sup>[20]</sup> Administration of *O. stamineus* at a dose of 1000 mg/kg can significantly reduce blood pressure in a rat model of spontaneous hypertension, by reducing the vasoconstrictive response by changing the activity of  $\alpha$ 1-adrenergic and AT1 receptors.<sup>[21]</sup>

***Moringa oleifera***

*Moringa oleifera* is a plant belonging to the *Moringaceae* family that is traditionally used as antiasthma, antidiabetic, hepatoprotective, anti-inflammatory, antifertility, anticancer, antimicrobial, antioxidant, cardiovascular, antiulcer, central nervous system activity, anti-allergy, wound healing, analgesic, and antipyretic.<sup>[22, 23]</sup> Administration of *M. oleifera* at a dose of 150–600 mg/kg/day for 30 days was reported to significantly reduce levels of total cholesterol, LDL, VLDL, triglycerides, and atherogenic index, as well as increase HDL levels and cholesterol excretion in feces in hyperlipidemia mouse models.<sup>[24]</sup>

***Punica granatum***

*Punica granatum* has been used as a traditional medicine for centuries in Indonesia. This plant has been shown to be rich in phenolic compounds such as flavonoids, ellagitannins, and anthocyanidins, as well as metabolites such as urolithin.<sup>[25]</sup> This plant has also been reported to have various pharmacological activities, including antioxidant, anti-inflammatory, antidiabetic, antiatherosclerotic, antihypertensive, antihyperlipidemic, antimicrobial, and anticancer activities.<sup>[26]</sup> Giving *P. granatum* juice to patients with unstable angina and myocardial infarction at a dose of 220 mL/day for 5 days has been reported to significantly reduce the intensity, incidence, and duration of angina pectoris in patients with unstable angina. Apart from that, there was also a decrease in serum troponin and malondialdehyde levels in myocardial infarction patients.<sup>[27]</sup>

***Sonchus arvensis***

*Sonchus arvensis*, or better known as Tempuyung leaf, is an annual herb that has single, clustered light green leaves that are thinner and tightly serrated, up to 2 meters high, soft stems, and are hollow and green in color. The flowers are in the form of panicles with smooth, loose crown strands and are yellow in color. This plant is reported to have many benefits, including antibacterial, antiviral, antihypertensive, and treatment of heart and blood vessel disorders.<sup>[28]</sup> Administration of *S. arvensis* leaf water fraction at a dose of 100 mg/kg was reported to significantly protect the myocardium and provide a cardioprotective effect in a mouse model of isoproterenol-induced myocardial infarction by inhibiting the production of TNF- $\alpha$ .<sup>[29]</sup>

***Centella asiatica***

*Centella asiatica* is a plant belonging to the *Apiaceae* family that is used as traditional medicine in several countries, including Indonesia. This plant is known to contain triterpenoids and saponins as the main elements, which are believed to be responsible for its wide therapeutic action, such as healing wounds, leprosy, lupus, varicose ulcers, eczema, psoriasis, diarrhea, fever, amenorrhea, and diseases of the genitourinary tract in women, as well as eliminating anxiety and improving cognition.<sup>[30, 31]</sup> Oral administration of *C. asiatica* extract at doses of 10 and 30 mg/kg for 7 weeks was reported to

prevent cardiac hypertrophy and cardiac fibrosis caused by pressure overload in mice through activation of AMPK $\alpha$  and inhibition of ERK and mTOR.<sup>[32]</sup>

***Morinda citrifolia***

*Morinda citrifolia* is commonly used in popular medicine in Indonesia. Many parts of the *M. citrifolia* tree are used in traditional medicinal practices, including the roots, leaves, and seeds. This plant has been reported to have various properties, including immunostimulatory, antitumor, antidiabetic, antiobesity, antibacterial and antiseptic, antifungal, antiviral, leishmanicidal, anti-inflammatory, antinociceptive and analgesic, antioxidant, neuroprotective, wound healing, antiallergic, antiangiogenic, antiemetic, antinausea, anti-gastric ulcer and esophagitis, anthelmintic, antimutagenic, antipsychotic, anxiolytic, photoprotective, and periodontal tissue regeneration activity.<sup>[33]</sup> Administration of *M. citrifolia* extract at doses of 100, 300, and 500 mg/kg for 20 days was reported to protect the heart from damage by reducing LDH and CK-MB levels in doxorubicin-induced rat models.<sup>[34]</sup>

***Averrhoa bilimbi***

*Averrhoa bilimbi* is a medicinal plant belonging to the *Oxalidaceae* family. *A. bilimbi* is a small tree that grows up to 15 m tall with sparsely arranged branches. It has compound leaves with twenty to forty leaflets each and a length of 5-10 cm. The leaves are hairy and pinnate and form bunches at the ends of the branches. The tree is cauliflower-shaped, with 18-68 flowers in panicles that form on the trunk and other branches. The flowers are heterostyle, with petals 10-30 m long, yellowish green to reddish purple in color. The fruit is produced on bare stems. The fruit is greenish with firm, juicy flesh that becomes soft when ripe. This plant has been used in traditional medicine for the treatment of various diseases, including as an antibacterial, astringent, postpartum protective medicine, treatment of fever, rectal inflammation, and diabetes.<sup>[35]</sup> Administration of *A. bilimbi* extract at a dose of 200 mg/kg for 13 days was reported to protect the heart from damage by reducing serum levels of CK-MB, LDH, and TBARS in heart tissue in a doxorubicin-induced mouse model. In addition, *A. bilimbi* also protects against DNA fragmentation in heart tissue.<sup>[36]</sup>

**CONCLUSION**

Many of the medicinal plants found in Indonesia have the potential to become alternative treatments for cardiovascular diseases. Experimental evidence and scientific testing have demonstrated the efficacy of each of these plants in the treatment of diverse cardiovascular diseases. These plants' active compounds, through various mechanisms, exert their cardioprotective effects. It is hoped that research on medicinal plants can be used to improve the treatment of cardiovascular disease.

## REFERENCES

1. Parikh H, Tripathi CB, Shah P, Pharm VGM, Goyal RK. Investigation of the cardioprotective effects of *Crataegus oxycantha* and its molecular mechanism. *Curr Res Cardiol*, 2015; 2(4): 161-167.
2. Patil SS, Naikwade NS, Shikalgar TS. The cardioprotective effect of argemone mexicana on isoproterenol induced cardiotoxicity in rats. *Eur J Pharm Med Res*, 2018; 5(6): 367-375.
3. 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.
4. Thounaojam MC, Jadeja RN, Ansarullah, Karn SS, Shah JD, Patel DK, *et al.* Cardioprotective effect of *Sida rhomboidea*. Roxb extract against isoproterenol induced myocardial necrosis in rats. *Exp Toxicol Pathol*, 2011; 63(4): 351-356.
5. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, *et al.* Heart disease and stroke statistics-2017 update: A Report from the American Heart Association. *Circulation*, 2017; 135(10): e146-e603.
6. Tesfaye BA, Berhe AH, Wondafrash DZ, Berhe DF. Cardioprotective effect of crude extract and solvent fractions of *Urtica simensis* leaves on cyclophosphamide-induced myocardial injury in rats. *J Exp Pharmacol*, 2021; 13: 147-160.
7. Wirtz VJ, Kaplan WA, Kwan GF, Laing RO. Access to medications for cardiovascular diseases in low- and middle-income countries. *Circulation*, 2016; 133(21): 2076-2085.
8. Chandrashekar BS, Prabhakara S, Mohan T, Shabeer D, Bhandare B, Nalini M, *et al.* Characterization of *Rubia cordifolia* L. root extract and its evaluation of cardioprotective effect in Wistar rat model. *Indian J Pharmacol*, 2018; 50(1): 12-21.
9. Amalia A, Romdon DS, Kusumawati N, Salsabila MA, Afifah ND, Shaomitha R, *et al.* Antihyperuricemia activities of several active compounds from medicinal plants: A review. *Eur J Biomed Pharm Sci*, 2024; 11(3): 15-18.
10. Nurhamidah W, Wijaya GD, Nurshazidah S, Zulfa AN, Chaerunnisa, Solihat S, *et al.* Anticoagulant activities of several active compounds from medicinal plants: A review. *Eur J Pharm Med Res*, 2024; 11(3): 13-16.
11. 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)Suppl: 1589-1593.
12. Setiawan MA, Fuadah TZ, Ningsih DU, Nabil M, Nababan A, Nurhabibah I, *et al.* The genus *Begonia* (*Begoniaceae*): A review of pharmacological studies. *Eur J Biomed Pharm Sci*, 2024; 11(3): 04-07.
13. Zulkarnaen P, Fadila N, Fadhilah LN, Kartika, Kardila K, Laely N, *et al.* Pharmacological activity of *Selaginella doederleinii* Hieron: An updated review. *Eur J Pharm Med Res*, 2024; 11(3): 17-20.
14. Alkandahri MY, Patala R, Berbudi A, Subarnas A. Antimalarial activity of curcumin and kaempferol using structure based drug design method. *J Adv Pharm Educ Res*, 2021; 11(4): 86-90.
15. Alkandahri MY, Arfania M, Abriyani E, Ridwanuloh D, Farhamzah, Fikayuniar L, *et al.* Evaluation of antioxidant and antipyretic effects of ethanolic extract of cep-cepan leaves (*Castanopsis costata* (Blume) A.DC). *J Adv Pharm Educ Res*, 2022; 12(3): 107-112.
16. 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.
17. 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.
18. Alkandahri MY, Yuniarsih N, Berbudi A, Subarnas A. Antimalaria activities of several active compounds from medicinal plants. *Pharmacogn J*, 2022; 14(1): 245-252.
19. Rahma S, Rhena EP, Adindika EAP, Widiyani F, Zahira G, Saraswati GAPPD, *et al.* Medicinal plants for treatment of idiopathic thrombocytopenic purpura: A review. *Eur J Biomed Pharm Sci*, 2024; 11(3): 08-10.
20. Ashraf K, Sultan S, Adam A. *Orthosiphon stamineus* Benth. is an outstanding food medicine: Review of phytochemical and pharmacological activities. *J Pharm Bioallied Sci*, 2018; 10(3): 109-118.
21. Manshor NM, Dewa A, Asmawi MZ, Ismail Z, Razali N, Hassan Z. Vascular reactivity concerning *Orthosiphon stamineus* Benth-mediated antihypertensive in aortic rings of spontaneously hypertensive rats. *Int J Vasc Med*, 2013; 2013: 1-8.
22. Paikra BK, Dhongade HKJ, Gidwani B. Phytochemistry and pharmacology of *Moringa oleifera* Lam. *J Pharmacopuncture*, 2017; 20(3): 194-200.
23. Andini DAP, Utami DSP, Puspawati I, Geralda AY, Apriani IP, Syalomita D, *et al.* Antidyslipidemic activity of some medicinal plants from Karawang, West Java, Indonesia: A review. *Eur J Pharm Med Res*, 2024; 11(3): 1-4.
24. Jain PJ, Patil SD, Haswani NG, Girase MV, Surana SJ. Hypolipidemic activity of *Moringa oleifera* Lam., Moringaceae, on high fat diet-induced hyperlipidemia in albino rats. *Braz J Pharmacogn*, 2010; 20(6): 969-973.
25. Fahmy HA, Farag MA. Ongoing and potential novel trends of pomegranate fruit peel; A comprehensive

- review of its health benefits and future perspectives as nutraceutical. *J Food Biochem*, 2022; 46(1): 1-19.
26. Singh B, Singh JP, Kaur A, Singh N. Phenolic compounds as beneficial phytochemicals in pomegranate (*Punica granatum* L.) peel: A review. *Food Chem*, 2018; 261: 75-86.
  27. Razani Z, Dastani M, Kazerani HR. Cardioprotective effects of pomegranate (*Punica granatum*) juice in patients with ischemic heart disease. *Phytother Res*, 2017; 31(11): 1731-1738.
  28. Wahyuni DK, Nariswari A, Supriyanto A, Purnobasuki H, Punnapayak H, Bankeeree W, *et al.* Antioxidant, antimicrobial, and antiplasmodial activities of *Sonchus arvensis* L. leaf ethyl acetate fractions. *Pharmacogn J*, 2022; 14(6)Suppl: 993-998.
  29. Kurniati NF, Sukandar EY, Rusnedi R, Ayuningtyas DK, Suliska N, Fujio Y. Water fraction of *Sonchus arvensis* (Linn.) leaves protects heart upon isoproterenol-induced myocardial infarction in rats and promotes survival of cardiomyocytes in vitro. *J Res Pharm*, 2019; 23(2): 242-248.
  30. 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.
  31. Budiyanti LE, Saputra MYKA, Wulandari SA, Amallia S, Azzahra AJ, Sagala BC, *et al.* Antihypertensive effects of some medicinal plants in Indonesia: A review. *Eur J Pharm Med Res*, 2024; 11(3): 5-8.
  32. Ma ZG, Dai J, Wei WY, Zhang WB, Xu SC, Liao HH, *et al.* Asiatic acid protects against cardiac hypertrophy through activating AMPK $\alpha$  signalling pathway. *Int J Biol Sci*, 2016; 12(7): 861-871.
  33. Torres MAO, Magalhães IFB, Mondêgo-Oliveira R, de Sá JC, Rocha AL, Abreu-Silva AL. One plant, many uses: A review of the pharmacological applications of *Morinda citrifolia*. *Phytother Res*, 2017; 31(7): 971-979.
  34. Lovin L, Lister INE, Fachrial E, Lie S. Cardioprotective effect of ethanolic extract of mengkudu (*Morinda citrifolia*) on rats induced by doxorubicin. *J Inv Bio Pharm Sci*, 2019; 4(4): 7-12.
  35. Alhassan AM, Ahmed QU. *Averrhoa bilimbi* Linn.: A review of its ethnomedicinal uses, phytochemistry, and pharmacology. *J Pharm Bioallied Sci*, 2016; 8(4): 265-271.
  36. Francis A, Nayak Y. Modulation of doxorubicin-induced cardiotoxicity by *Averrhoa bilimbi* extract. *J Young Pharm*, 2017; 9(1): 69-77.