International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 14, Special Issue 1, 2022

Review Article

REVIEW OF ANTIHYPERTENSIVE ACTIVITIES OF THREE SPECIES OF *ZINGIBERACEAE*

DESI NADYA AULENA[1], RASYIIDA NUUR RAAFI[1], NIKO SAMUEL[1], YESI DESMIATY[1*], RISMA MARISI TAMBUNAN[1], DIAH KARTIKA PRATAMI[1]

[1]Faculty of Pharmacy, Pancasila University, Srengseng Sawah, Jagakarsa, South Jakarta, 12640, Indonesia
[*]Email: yesi.desmiaty@univpancasila.ac.id

Received: 10 Nov 2021, Revised and Accepted: 15 Dec 2021

ABSTRACT

Objective: The purpose of this study was aimed to review the antihypertensive activities of 3 plant species from the Familia Zingiberaceae.

Methods: This review examined the antihypertensive activities by obtaining data from primary, secondary, and tertiary articles on journal sites such as Google Scholar, PubMed, Wiley Online Library, Elsevier, Springer, ResearchGate with a maximum publication of 10 y and contains relevant bibliographies.

Results: Literature studies has shown that white ginger (*Zingiber officinale* Roscoe) is clinically effective as an antihypertensive agent by lowering systolic blood pressure and serum sICAM-1 concentration. Furthermore, the *in vivo* administration lowers the blood pressure in the arteries of anesthetized rats while *in vitro* demonstrated a dose-dependent ACE inhibitory activity. *Curcuma javanica* (*Curcuma xanthorrhiza* Roxb) also has a similar effect with changes in the respondent's systolic and diastolic blood pressure, and when administered *in vivo*, it reduces renin levels in the adjuvant captopril group than the negative control group while *in vitro* administration showed high ACE inhibitory activity. Aromatic ginger (*Kaempferia galanga* L) administered *in vivo* lowered the basal arterial pressure (MAP) and increased diuretic activity depending on the urine volume dose and the excretion of $Na^+$and K^+.

Conclusion: Based on the results, plants in the Zingiberaceae family, namely white ginger (*Zingiber officinale* Roscoe), *Curcuma javanica* (*Curcuma xanthorrhiza* Roxb), and aromatic ginger (*Kaempferia galanga* L) have antihypertensive activities clinically, *in vivo*, and *in vitro*.

Keywords: Antihypertensive, Zingiberaceae, Angiotensin-converting Enzyme, *Zingiber oficinale* roscoe, *Curcuma xanthorrhiza* roxb, *Kaempferia galanga L.*

DOI: https://dx.doi.org/10.22159/ijap.2022.v14s1.14 Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Indonesia has the second-largest biodiversity in the world after Brazil with approximately 25,000 to 30,000 plant species and 9,000 are medicinal. Meanwhile, plants from the Zingiberaceae family have many properties such as antihypertensive, antibacterial, anti-inflammatory, analgesic, and antioxidant effects [1]. Furthermore, to provide a good therapeutic effect, it is necessary to carry out a standardization process to ensure the quality and efficacy of the drug produced from medicinal plant [2]. Standardization is a set of parameters, procedures, and measurement methods used in determining the pharmaceutical quality paradigm, quality in terms of standard requirements (chemical, biological, and pharmaceutical), and stability limits of pharmaceutical products. Also, it plays an important role in guaranteeing Indonesian herbal medicines, especially during the production of standardized herbal medicines (OHT) and phytopharmaceuticals [3]. Generally, the production of traditional medicine follows the same principle as its synthetic counterpart. Simplicia or extracts used as raw materials needs to meet general standard parameters (moisture content, ash content, dry loss, specific gravity), specific standard parameters (organoleptic, solute compounds in solvents), and certain tests such as chemical content test. Plant metabolomic profile (metabolic profiling) is an important parameter used in standardization as well as the plant metabolism used to determine the secondary metabolite content of plants [4].

Hypertension is a degenerative disease with a high mortality rate diagnosable with systolic blood pressure. A person is said to be hypertensive when the systolic blood pressure ≥ is 140 mmHg and/or the diastolic blood pressure ≥ is 90 mmHg on repeated examinations. Several plants in Indonesia have been widely used as a therapeutic intervention for the treatment of hypertension, such as white ginger *(Zingiber officinale Roscoe*), *Curcuma javanica (Curcuma xanthorrhiza Roxb),* and aromatic ginger (*Kaempferia galanga L*) [5, 6].

Furthermore, the disease is associated with oxidative stress due to the weak protective effect of the body's antioxidants. Increased oxidative stress lowers the bioavailability of nitric oxide (NO), thereby leading to hypertension. Exposure to free radicals increases the blood pressure of hypertensive patients; consequently, adequate antioxidant capacity is needed to reduce the levels of Reactive Oxygen Species (ROS) which inhibits the oxygen flow to the heart and brain to prevent lipid oxidation that causes atherosclerosis [6].

Z. officinale has a high antioxidant activity which includes the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging and methyl linoleate oxidation inhibition activity using the oil stability index (OSI) method while *C. xanthorrhiza* contains phenolic antioxidants, as well as NO inhibitory activity [7-9]. Meanwhile, antihypertensive drugs used widely are *angiotensin-converting enzyme* (ACEI) inhibitors which lower or prevent the formation of angiotensin II that increases blood pressure [6]. Balasuriya and Rupasinghe (2011) stated that plants containing flavonoids from the flavone group, flavonols, anthocyanins, isoflavones, and polyphenols such as hydrolyzed tannins, xanthone, procyanidin inhibits *Angiotensin-Converting Enzyme* (ACE) [5]. Subsequently, this study aims to review the antihypertensive activities of 3 plant species in the Zingiberaceae family, namely white ginger (*Zingiber officinale* Roscoe), Curcuma javanica (*Curcuma xanthorrhiza* Roxb), and aromatic ginger (*Kaempferia galanga* L).

Literature review methods

The study examined the antihypertensive activities of three plant species in the Zingiberaceae family, namely white ginger (*Zingiber officinale* Roscoe), *Curcuma javanica* (*Curcuma xanthorrhiza* Roxb), and aromatic ginger (*Kaempferia galanga* L). The study data were obtained from primary, secondary, and tertiary articles on journal sites such as Google Scholar, PubMed, Wiley Online Library, Elsevier, Springer, ResearchGate with a maximum of publication of 10 y and contains relevant bibliographies. The Literature review analysis was conducted using the C3S2 concept.

1. Finding Equations (Compare)
2. Looking for Dissimilarity (Contrast)
3. Giving Views (Criticism)
4. Comparing (Synthesizing)
5. Summarizing

The materials used for the review were results of the thesis, e-books, research journals on the pharmacological activities, efficacy, content, and chemical structure of the three chosen plant species in the Zingiberaceae family which have been officially published. The journals used were 14 manuscripts consisting of 11 International Journals, 1 National Journal, and 2 Thesis books.

White ginger (*Zingiber officinale* Roscoe)

Plant Classification [9].

- Division: Magnoliophyta (Spermatophyta)
- Subdivision: Magnoliophytina (Angiospermae)
- Class: Lilianae (Monocotyledoneae)
- Order: Zingiberales
- Family: Zingiberaceae
- Genus: Zingiber Mil
- Species: *Zingiber officinale* Roscoe

It has synonym name *Zingiber majus* Rumph [9]**.** It has the other name Zingiberis rhizome [9]**.** The chemical content of the rhizome of *Zingiber officinale* Roscoe are flavonoids, polyphenols, resin, starch, and fiber. It also contains essential oils consisting of n-nonylaldehyde, d-camphene, da-phellandrene, methyl heptanone, cineol, d-borneol, geraniol, linalool, acetates, caprylate, citral, chavicol, zingiberene [9, 10].

Efficacy and usability

The rhizome of Z. officinale is efficacious as a stomach laxative, cough medicine, rheumatism medicine, antidote, breast milk smoother, and appetite stimulator. It also serves as an intervention for heartburn, flatulence, sherbet, itching (external medicine), wounds (external medicine), headache (external medicine), and colds (external medicine) [10, 11].

Pharmacological activity of white ginger (*Zingiber officinale* roscoe)

In a clinical study by Azimi *et al.* (2016) that used 3 grams of ginger powder and 3 cups of black tea (Golestan, Tehran, and Iran) on patients with type 2 diabetes mellitus (age 30 y and BMI = 25 kg/m^2) for 8 w observed a reduction of the systolic blood pressure and serum sICAM-1 concentrations with no effect on diastolic blood pressure [12].

Furthermore, an *in vivo* study by Ghayur *et al.* (2005) used 70% methanol extract on rats and showed that *Z. officinale* Roscoe extracts at a dose of 0.3-3 mg/kg reduces arterial blood pressure in anesthetized rats [13], this agrees with Sanghal *et al.* (2011) that the use of *Z. officinale* and a high-fat diet (HFD) at a dose of 500 mg/kg BW in adult Wistar rats showed a good preventive effect of *the* extract against hypertension because the blood pressure was lower than the control group (HFD only) [14]. Manosroi *et al.* (2013) used an aqueous extract of white ginger rhizome and prazosin hydrochloride (positive control) at a dose of 10 mg/kg BW in male white Sprague-Dawley rats and showed that the extract had an antihypertensive activity with a decrease in the percentage of arterial blood pressure by 27.17±3.17% with a value 2.41 times that of prazosin hydrochloride as a standard drug [15]. Also, Rahmah NA. (2018) used 70% ethanol extract of *Z. officinale* Roscoe rhizome on male Sprague-Dawley strain rats with a dose of 500 mg/kgBW, which showed a significant decrease in systolic blood pressure compared to the negative control with a 27.35% decrease [16].

Meanwhile, an *in vitro* study by Ranilla *et al.* (2010) used an aqueous extract of *Z. officinale* Roscoe to study subjects with hippuric acid levels, results of HHL and ACE showed that the extract possesses relevant ACE inhibitory activity (56% in 2.5 mg dry sample) [17]. This agrees with a similar study by Rani *et al.* (2012) that used ethyl acetate extract of *Z. officinale* rhizome on hippuric acid levels and observed that the extract had a dose-dependent ACE inhibitory activity [18]. Akinyemi *et al.* (2013) used an aqueous extract of *Z. officinale* Roscoe and *Z. officinale* Rubrum at a dose of 25-125 µg/ml on hippuric acid levels in the study subject; the results of HHL and ACE of isolated rat heart showed that both varieties inhibit ACE and protect the heart from Fe2+and SNP-induced lipid peroxidation. However, Z. *officinale* Rubrum extract showed a stronger ACE inhibition than *Z. officinale* Roscoe extract [19]; this discovery agrees with Akinyemi *et al.* (2014) that used a supplement substance of the 2 varieties of *Z. officinale* in a high cholesterol diet to study the hippuric acid levels of albino Wistar rats and stated that *Z. officinale* Roscoe inhibited ACE better than *Z. Officinale* Rubrum [20].

Tumeric rhizome *Curcuma javanica* (*Curcuma xanthorrhiza* roxb.)

Plant classification [21]

- Division: Magnoliophyta (Spermatophyta)
- Subdivision: Magnoliophytina (Angiospermae)
- Class: Lilianae (Monocotyledoneae)
- Order: Zingiberales
- Family: Zingiberaceae
- Genus: Curcuma
- Species: *Curcuma xanthorrhiza* Roxb.

It has synonym name *Curcuma javanica* [21]**.** The other names are Curcumae Rhizoma or Curcumae javanicae Rhizoma [21]**.** The chemical content of the rhizome of *Curcuma xanthorrhiza* Roxb are saponins, flavonoids, essential oils, curcumin, starch, and xanthorhizol [21, 22].

Efficacy and usability

C. xanthorrhiza inhibits blood clotting, lowers cholesterol levels, which affects blood pressure and it has a pharmacological effect on active substances such as germacron that has anti-inflammatory effects and inhibits edema (swelling). It is also efficacious as breast milk smoother, body freshener, stomach reliever, seizure medicine, choleretic, cholagogic, anti-inflammatory, and antipyretic agent [7, 21, 22].

Pharmacological activity of *Curcuma javanica* (*Curcuma xanthorrhiza* Roxb.)

A clinical study by Fitriani DT (2013) using *C. xanthorrhiza* powder at a dose of 25 mg once per day for 1 w on study subjects consisting of 12 respondents with an age range of 65-75 y showed changes in respondent's systolic and diastolic blood pressure before and after administration of *C. xanthorrhiza* [23].

An *in vivo* study by Priyadi *et al.* (2015) using 96% ethanol extract of *C. xanthorrhiza* rhizome on male rats (*Mus musculus*) subjects showed that renin levels in the captopril adjuvant group were lower than the negative control group but higher than the normal and positive control group [24].

Furthermore, Saputri *et al.* (2015) used methanol extract of *C. xanthorrhiza* rhizome on study subject's hippuric acid levels observed high ACE inhibitory activity with an inhibition percentage of 71.1% [20].

Aromatic ginger (*Kaempferia* galanga L.)

Plant classification [25]

- Division: Magnoliophyta (Spermatophyta)
- Subdivision: Magnoliophytina (Angiospermae)
- Class: Lilianae (Monocotyledoneae)

- Order: Zingiberales
- Family: Zingiberaceae
- Genus: Kaempferia
- Species: *Kaempferia galanga* L.

It has synonym name *Kaempferia galanga* L. [25]**.** The other name is Kaempferiae Rhizoma [25]**.** The chemical content of the rhizome of *Kaempferia galanga* L. are saponins, flavonoids, starch, hars, and polyphenols while the essential oil consists of borneol, methyl-p-cumaric, acid, cinnamic acid ethyl ester, pentadecane, cinnamic aldehyde, and camphene [25].

Efficacy and usability

K. galanga L. helps to treat dysentery, gout, aches and pains, stomach pain, cough, bloating, swelling (external medicine), ulcers, tetanus, vomiting, and mushroom poisoning [25].

Pharmacological activity of aromatic ginger (Kaempferia galanga L.)

An *in vivo* study by Othman *et al.* (2006) that used the rhizome extract of *K. galanga* L. dichloromethane at a dose of 10; 33; 100 mg/ml in male Wistar rats showed that an increase in the extract in anesthetized rats exhibited hypotensive properties as it lowers the basal arterial pressure (MAP) with a maximal effect seen after 5-10 min of injection [26]. This is in line with Mohammad *et al.* (2016) that used petroleum ether extract of *K. galanga* L. rhizome at a dose of 200 mg/kg and 400 mg/kg with furosemide (positive control) in Wistar rat (2 sexes). The result showed an increase of diuretic activity that depends on urine volume and excretion of $Na^+$and K^+ [27].

CONCLUSION

Plants from the Zingiberaceae family, namely white ginger (*Zingiber officinale Roscoe*), Curcuma javanica (*Curcuma xanthorrhiza Roxb*), and aromatic ginger (*Kaempferia galangal L.*) have shown antihypertensive activity clinically, *in vivo* and *in vitro*.

ACKNOWLEDGEMENT

This article is part of the study independent of MBKM Pancasila University. The authors are grateful to the Ministry of Education, Culture and Higher Education, Republic of Indonesia for the financial support through the Matching Fund Grant 2021.

FUNDING

This review was funded by the Ministry of Education and Culture, Republic of Indonesia through the Matching Fund Grant (MoU No: 2761/E3/PKS. O7/KL/2021 and No: 4970/R. UP/PKS/VIII/2021).

AUTHORS CONTRIBUTIONS

All the authors contributed equally.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

REFERENCES

1. Wandita GA, Musrifoh I. Review artikel: tanaman suku Zingiberaceae Y. Memiliki Aktivitas Sebagai Antioksidan. Farmaka. 2018;16:564-71.
2. R. H D. Pengembangan obat tradisional Indonesia menjadi fitofarmaka. Maj Kedokt Indones. 2007;57:205-10.
3. Departemen Kesehatan RI. Parameter standar umum ekstrak tanaman obat. Departemen Kesehatan RI. 2000;1:10-1.
4. Utami YP, Umar AH, Syahruni R, Kadullah I. Standardisasi simplisia dan ekstrak etanol daun leilem [*Clerodendrum minahassae* Teisjm. and Binn.]. J Pharm Sci. 2017;2:32-9.
6. BB, HR. Plant flavonoids as angiotensin-converting enzyme inhibitors in regulation of hypertension. Funct Foods Heal Dis. 2011;1:172-88.
7. Hansen K, Nyman U, Smitt UW, Adsersen A, Gudiksen L, Rajasekharan S, Pushpangadan P. *In vitro* screening of traditional medicines for anti-hypertensive effect based on inhibition of the angiotensin-converting enzyme (ACE). J Ethnopharmacol. 1995;48(1):43-51. doi: 10.1016/0378-8741(95)01286-m, PMID 8569246.
8. Putri R, Mursiti S, Sumarni W. Aktivitas antibakteri kombinasi temu putih dan temulawak terhadap streptococcus mutans. J MIPA. 2017;40:43-7.
9. Febriyanti RM, Maesaroh I, Supriyatna S, Sukandar H, Maelaningsih FS. Pharmacoeconomics analysis of scientification of antihypertensive, antihyperglycemic, antihypercholesterolemic, and antihyperuricemic Jamu. IJPST. 2014;1(2):39-46. doi: 10.15416/ijpst.v1i2.7512.
10. Syafitri DM, Levita J, Mutakin M, Diantini A. A review: is ginger (*Zingiber officinale* var. Roscoe) potential for future phytomedicine? Indones J Appl Sci. 2018;8:1-10.
11. Mao QQ, Xu XY, Cao SY, Gan RY, Corke H, Beta T, Li HB. Bioactive compounds and bioactivities of ginger (*Zingiber officinale* roscoe). Foods. 2019;8(6):1-21. doi: 10.3390/foods8060185, PMID 31151279.
12. Liu Y, Liu J, Zhang Y. Research progress on chemical constituents of *Zingiber officinale* roscoe. BioMed Res Int. 2019;2019:5370823. doi: 10.1155/2019/5370823, PMID 31930125.
13. Azimi P, Ghiasvand R, Feizi A, Hosseinzadeh J, Bahreynian M, Hariri M, Khosravi Boroujeni H. Effect of cinnamon, cardamom, saffron and ginger consumption on blood pressure and a marker of endothelial function in patients with type 2 diabetes mellitus: a randomized controlled clinical trial. Blood Press. 2016;25(3):133-40. doi: 10.3109/08037051.2015.1111020, PMID 26758574.
14. Ghayur MN, Gilani AH. Ginger lowers blood pressure through blockade of voltage-dependent calcium channels. J Cardiovasc Pharmacol. 2005;45(1):74-80. doi: 10.1097/00005344-200501000-00013, PMID 15613983.
15. Nath R. An experimental study to evaluate the preventive effect of *Zingiber officinale* (ginger) on hypertension and hyperlipidaemia and its comparison with Allium sativum (garlic) in rats. J Med Plants Res. 2011;6:4231-8.
16. Manosroi A, Lohcharoenkal W, Khonsung P, Manosroi W, Manosroi J. Potent antihypertensive activity of Thai-Lanna medicinal plants and recipes from "Manosroi III" database. Pharm Biol. 2013;51(11):1426-34. doi: 10.3109/13880209.2013.796391, PMID 23869399.
17. Rahmah NA. Skrining aktivitas antihipertensi dari ekstrak etanol 70% rimpang: jahe merah (*Zingiber officinale* roscoe), bangle (*Zingiber purpureum* Roscoe), temu kunci (*Boesenbergia rotunda* (L.) Mansf.) dan temu putih (*Kaempfria rotunda* L.) pada tikus yang diinduksi adrenalin. J Chem Inform Model. 2013;53.
18. Ranilla LG, Kwon YI, Apostolidis E, Shetty K. Phenolic compounds, antioxidant activity and *in vitro* inhibitory potential against key enzymes relevant for hyperglycemia and hypertension of commonly used medicinal plants, herbs and spices in latin America. Bioresour Technol. 2010;101(12):4676-89. doi: 10.1016/j.biortech.2010.01.093, PMID 20185303.
19. Rani MP, Krishna MS, Padmakumari KP, Raghu KG, Sundaresan A. *Zingiber officinale* extract exhibits antidiabetic potential via modulating glucose uptake, protein glycation and inhibiting adipocyte differentiation: an *in vitro* study. J Sci Food Agric. 2012;92(9):1948-55. doi: 10.1002/jsfa.5567, PMID 22261727.
20. Akinyemi AJ, Ademiluyi AO, Oboh G. Aqueous extracts of two varieties of ginger (*Zingiber officinale*) inhibit angiotensin I-converting enzyme, iron(II), and sodium nitroprusside-induced lipid peroxidation in the rat heart *in vitro*. J Med Food. 2013;16(7):641-6. doi: 10.1089/jmf.2012.0022, PMID 23875904.
21. Akinyemi AJ, Ademiluyi AO, Oboh G. Inhibition of angiotensin-1-converting enzyme activity by two varieties of ginger (*Zingiber officinale*) in rats fed a high cholesterol diet. J Med Food. 2014;17(3):317-23. doi: 10.1089/jmf.2012.0264, PMID 24433069.
22. Hwang J, Rukayadi Y. Challenges and opportunities in applying temulawak (*Curcuma xanthorrhiza* Roxb.) for industrial oral care products. Bogor Agric Univ 2006 (July):25-32.

23. Yamada K, Subeki, Nabeta K, Yamasaki M, Katakura K, Matsuura H. Isolation of antibabesial compounds from Brucea javanica, curcuma xanthorrhiza, and Excoecaria cochinchinensis. Biosci Biotechnol Biochem. 2009;73(3):776-80. doi: 10.1271/bbb.80784, PMID 19270401.
24. Fitriani DT. Efektifitas temulawak dalam menurunkan tekanan darah pada lansia di upt panti sosial tresna werdha mulia dharma kabupaten kubu raya. SSRN Electron J. 2013;1.
25. Priyadi M, Yusetyani L HD. Pengaruh pemberian ekstrak temulawak (Curcuma *xanthorrhiza* Roxb.) sebagai adjuvan terapi captopril terhadap Kadar renin pada mencit jantan (*Mus musculus*) yang diinduksi hipertensi; 2013.
26. Megantara S, Farmasi F, Padjadjaran U, Farmakologi A. Karakteristik morfologi bunga kencur (*Kaempferia galanga* L.). Boll Penelit Tanam Rempah Obat. 2016;19:109-16.
27. Othman R, Ibrahim H, Mohd MA, Mustafa MR, Awang K. Bioassay-guided isolation of a vasorelaxant active compound from Kaempferia galanga L. Phytomedicine. 2006;13(1-2):61-6. doi: 10.1016/j.phymed.2004.07.004, PMID 16360934.