

ANTIHYPERTENSIVE POTENTIAL OF FLAVONOID-CONTAINING MEDICINAL PLANTS: A NARRATIVE REVIEW

Kadek Diah Lestari Kencana¹, Ni Made Pitri Susanti^{1*}

¹Department of Pharmacy, Faculty of Mathematics and Natural Science, Udayana University
Bali 80361, Indonesia

Corresponding author email: dekpitsusanti@unud.ac.id

ABSTRACT

Background: Hypertension is a prevalent chronic disease and a major cause of cardiovascular morbidity and mortality. Flavonoid-containing medicinal plants have attracted attention as potential natural antihypertensive agents. **Objective:** This review summarizes the antihypertensive potential of flavonoid-containing medicinal plants and their underlying mechanisms. **Methods:** A narrative literature review was conducted using PubMed and Google Scholar. Original articles published between 2015 and 2024 were selected based on predefined inclusion and exclusion criteria. Eligible studies investigated flavonoid-containing medicinal plants using *in silico*, *in vitro*, *ex vivo*, or animal models. Ten studies were included for qualitative analysis. **Results:** The reviewed plants contained flavonoids, including quercetin, kaempferol, luteolin, and rutin, which exhibited antihypertensive potential through ACE inhibition, enhanced nitric oxide bioavailability, and antioxidant activity. Evidence varied across molecular docking, laboratory, and animal studies. **Conclusion:** Flavonoid-containing medicinal plants are promising preclinical antihypertensive candidates; however, further pharmacological and clinical studies are required to confirm their efficacy and safety.

Keywords: Flavonoids; Herbal Medicines; Hypertension; Medicinal Plants; Phytopharmaceuticals

INTRODUCTION

Hypertension is a condition characterized by a systolic blood pressure of ≥ 130 mmHg and/or a diastolic blood pressure of ≥ 80 mmHg^[8]. Hypertension is widely regarded as a silent killer, given its contribution to an estimated annual mortality rate of approximately 13.5%, with the majority of deaths being attributable to cardiovascular complications, including coronary heart disease, stroke, and heart failure^[4].

As a condition with a high potential to cause mortality, hypertension requires prompt management through both

pharmacological and non-pharmacological approaches. Pharmacological treatment involves the administration of antihypertensive agents, including *Angiotensin Converting Enzyme (ACE) Inhibitors*, *Angiotensin Receptor Blockers (ARBs)*, *diuretics*, *Calcium Channel Blockers (CCBs)*, and *Beta-Blockers (BBs)*, which are given with consideration of patient-specific factors such as age, body weight, and comorbidities^[8]. However, long-term use of antihypertensive drugs may lead to adverse effects such as dry cough, gastrointestinal disturbances, edema, hypokalemia, and others^[3]. Therefore, there

is a growing tendency among the population to consider the use of natural products as alternative therapeutic options in the management of hypertension. This is corroborated by the World Health Organization (WHO), which estimates that up to 65% of the population in developed countries relies on traditional medicine and natural product-based therapies^[9].

Medicinal plants contain various bioactive secondary metabolites, among which flavonoids are one of the most extensively studied due to their potential antihypertensive properties. Experimental studies have demonstrated that flavonoids may lower blood pressure through multiple mechanisms, including inhibition of angiotensin-converting enzyme (ACE), enhancement of nitric oxide (NO) bioavailability, antioxidant activity, and improvement of endothelial function. These complementary mechanisms suggest that flavonoid-containing medicinal plants represent promising sources of natural antihypertensive agents. However, current evidence remains largely preclinical and has not yet been comprehensively synthesized.

Despite the growing number of studies on medicinal plants with antihypertensive activity, the available evidence is heterogeneous with respect to experimental design and biological models, highlighting the need for a comprehensive narrative synthesis. This review aims to summarize and critically discuss current preclinical evidence regarding flavonoid-containing medicinal plants with antihypertensive potential, focusing on their major flavonoid constituents, proposed mechanisms of action, and the strength of evidence derived from *in silico*, *in vitro*, *ex vivo*, and animal studies.

METHODS

This study employed a narrative literature review approach. Literature was searched through PubMed and Google Scholar databases between January and March 2025 using combinations of the keywords "*medicinal plants*," "*flavonoids*," "*hypertension*," "*antihypertensive*," "*ACE inhibitor*," and "*blood pressure*" connected using Boolean operators (AND/OR).

The inclusion criteria were original research articles published in English or Indonesian between 2015 and 2024 that investigated medicinal plants containing flavonoids and evaluated antihypertensive activity using *in silico*, *in vitro*, *ex vivo*, or animal models. Studies were also required to report flavonoid constituents and antihypertensive mechanisms. Exclusion criteria included review articles, conference proceedings, duplicate publications, studies without flavonoid identification, studies lacking antihypertensive evaluation, and articles with inaccessible full texts.

The literature selection process consisted of identification, title and abstract screening, full-text eligibility assessment, and final inclusion. At each stage, studies that did not satisfy the predefined inclusion criteria or met the exclusion criteria were excluded. Ultimately, ten studies fulfilled all eligibility criteria and were included in the qualitative narrative synthesis.

RESULTS

Based on the literature search conducted, a total of ten scientific articles were identified. The retrieved studies investigated various natural products containing flavonoids that are presumed to possess potential as antihypertensive agents.

Articles concerning flavonoid content in plants with potential antihypertensive activity are presented in Table 1.

Table 1. Flavonoid Content in Plants with Potential Antihypertensive Activity

Plant Name	Chemical Metabolites	Research Methods	Main Findings	Conclusion	References
<i>Ajuga integrifolia</i>	Quercetin, Rutin, Myricetin, Kaempferol, Repetoside	<i>In silico</i> , molecular docking, HPLC	Flavonoids (rutin, quercetin) are more efficacious than enalapril.	Flavonoids from <i>A. integrifolia</i> are effective as antihypertensive agents.	[16]
<i>Annona muricata</i>	Phenolic compounds, flavonoids	<i>In vitro</i> enzymatic assay	The pericap effectively inhibits ACE and diabetes-related enzymes.	Phenolic compounds are effective against hypertension and diabetes.	[1]
<i>Crinum zeylanicum</i>	Polyphenol and flavonoid	L-NAME-induced hypertensive rat model	The extract reduces blood pressure and improves renal function.	<i>C. zeylanicum</i> is effective as a therapy for hypertension and renal protection.	[11]
<i>Limonia acidissima</i>	Flavonoid, Tannin, Alkaloid	<i>In silico</i> network pharmacology	ACE, NOS3, and EDNRA genes as therapeutic targets	<i>Limonia acidissima</i> shows potential as a genetically based antihypertensive therapy.	[13]
<i>Citrullus colocynthis</i>	Quercetin, Myricetin, Ferulic acid, Chlorogenic acid	SHR model, HPLC-MS, antioxidant	Ethyl acetate fraction (EAF) reduces blood pressure and oxidative stress.	<i>C. colocynthis</i> EAF is effective as an antihypertensive agent.	[7]
<i>Amaranthus cruentus</i>	Catechin, Quercetin, Kaempferol, Naringenin, Ferulic acid	HPLC-UV-DAD, <i>in vitro</i> , <i>ex vivo</i> , molecular docking	Leaf extract reduces ACE activity and induces aortic relaxation by 45%.	<i>A. cruentus</i> has potential as a functional food with antihypertensive properties.	[2]
<i>Persea americana</i>	Flavonoid (not specified)	Rat model, tail-cuff method, NaCl+prednisone	A dose of 375 mg/kg body weight reduces blood pressure by up to 48%/41%.	Avocado extract is as effective as captopril.	[12]

Plant Name	Chemical Metabolites	Research Methods	Main Findings	Conclusion	References
<i>Boerhavia diffusa</i>	Eupalitin 3-O-β-D-galactopyranoside	Molecular docking, rat model	The compound significantly reduces blood pressure.	Eupalitin 3-O-β-D-galactopyranoside shows potential as an antihypertensive agent.	[17]
<i>Brassica oleracea</i>	Total flavonoid content: 8.622 mg QE/g	Wistar rat model, NIBP	A dose of 400 mg/kg body weight is effective in reducing blood pressure.	Cabbage extract effectively reduces blood pressure in experimental animals.	[14]
<i>Psidium guajava</i> L.	Flavonoids (luteolin, kuersetin, kaempferol, etc.)	<i>In silico</i> (docking, farmakofor, ADMET)	Luteolin and chlorogenic acid exhibit strong binding affinity to ACE and favorable ADMET profiles.	Guava leaf flavonoids show potential as natural antihypertensive agents.	[6]

The study conducted by Tessema *et al.* (2024) evaluated flavonoids from *Ajuga integrifolia* to support their potential antihypertensive application, utilizing an *in silico* framework based on molecular docking analysis and biological activity prediction through the *Prediction of Activity Spectra for Substances* (PASS) approach. Flavonoids such as *quercetin*, *myricetin*, *rutin*, and *kaempferol* were identified via HPLC from the methanolic extract of the aerial parts of the plant, and subsequently evaluated for their activity against the ACE enzyme as a primary target in hypertension therapy. The docking results demonstrated strong binding affinity values ranging from -10.5 to -8.7 kcal/mol, which were lower than that of the reference drug enalapril (-5.9 kcal/mol), with the compounds also exhibiting low inhibition constant (K_i) values, indicating high efficacy in ACE inhibition. These flavonoids establish hydrogen bonds with key active-site residues of ACE, including Tyr523, His353, and Glu384, which are critically involved in the conversion of angiotensin I to angiotensin II, thereby, ACE inhibition promotes vasodilation and

consequently leads to a reduction in blood pressure. In addition, PASS results indicated that these flavonoids exhibit a probability of vasoprotective and vasodilatory activity exceeding 0.7, indicating their potential to promote vascular dilation and protect the endothelium from oxidative stress-induced damage, which is highly relevant to hypertension therapy. The flavonoid constituents of *A. integrifolia* also satisfy drug-likeness parameters with minimal Lipinski's rule violations, although gastrointestinal absorption remains to be optimized, indicating their potential for development as natural product-based antihypertensive drug candidates.

The study conducted by Adefegha *et al.* (2015) aimed to evaluate the antihypertensive potential of aqueous extracts from different parts of *Annona muricata* (soursop), including the pericarp, pulp, and seeds, with a primary focus on the inhibition of *Angiotensin-Converting Enzyme* (ACE), a key enzyme in blood pressure regulation. The methods employed encompassed extract preparation through aqueous maceration (1:100 w/v), followed

by evaluation of *in vitro* ACE inhibitory activity using spectrophotometric analysis, along with the assessment of phenolic content and antioxidant activity to elucidate the underlying mechanism of action. The results demonstrated that the pericarp extract exhibited the strongest ACE inhibitory activity, with an IC_{50} value of 0.03 mg/mL, compared to the pulp and seed extracts. This efficacy is attributed to the highest total phenolic content observed in the pericarp, reaching 560.21 mg/100 g, with flavonoids serving as the principal contributing components. Flavonoids in *A. muricata* are believed to reduce blood pressure through two principal mechanisms, namely inhibition of ACE activity leading to decreased production of angiotensin II, a potent vasoconstrictor, as well as antioxidant activity that protects the vascular endothelium from oxidative damage. The combined enzymatic inhibitory and antioxidant activity further reinforces the potential of flavonoids from *A. muricata*, particularly those present in the fruit pericarp, as efficacious natural antihypertensive agents.

The study conducted by Ndjenda *et al.* (2021) evaluated the antihypertensive effects of methanolic extracts and the ethyl acetate fraction of *Crinum zeylanicum* leaves using an L-NAME-induced hypertensive rat model in which L-NAME inhibits *nitric oxide* (NO) synthesis, resulting in endothelial dysfunction and elevated blood pressure. The extract was administered at three dose levels (30, 60, and 120 mg/kg body weight) over a three-week period, with parameters assessed including blood pressure, heart rate, plasma NO levels, and renal function biomarkers. The results indicated that the ethyl acetate fraction (LEAF) exhibited the highest flavonoid content and the strongest antioxidant activity compared to other fractions. Administration with this fraction

significantly lowered blood pressure, elevated plasma NO levels, and enhanced renal function. This finding indicates that flavonoids in *C. zeylanicum* play a central role in lowering blood pressure through vasodilatory mechanisms mediated by enhanced NO bioavailability. Furthermore, the antioxidant activity of flavonoids contributes to the attenuation of oxidative stress and preserves the integrity of the vascular endothelium against damage. Accordingly, the high flavonoid content in the ethyl acetate fraction of *Crinum zeylanicum* represents a key factor underlying the antihypertensive therapeutic effects of this plant.

The study conducted by Pertiwi *et al.* (2024) employed an *in silico* and network pharmacology approach to explore the antihypertensive potential of *Limonia acidissima*, focusing on the identification and mapping of interactions of 47 secondary metabolites with key protein targets involved in blood pressure regulation, including ACE, NOS3, and EDNRA. Based on these metabolites, flavonoids represent one of the major groups exhibiting high affinity toward these biological targets. Flavonoids are known to inhibit ACE activity and enhance endothelial *Nitric Oxide Synthase* (eNOS) activity, thereby promoting nitric oxide (NO) release and inducing vasodilation. Further Gene Ontology and KEGG analyses indicated that flavonoids in *L. acidissima* are involved in key signaling pathways, including *cGMP-PKG*, *HIF-1*, and other hormonal regulatory pathways associated with blood pressure regulation. This multi-target mechanism suggests that flavonoids from *L. acidissima* do not merely act as single agents in lowering blood pressure but also play an integral role in maintaining vascular homeostasis through their influence on enzymatic systems, cellular signaling pathways, and

oxidative status. Accordingly, flavonoids from this plant serve as key components that reinforce the potential of *L. acidissima* as a phytochemical-based antihypertensive therapeutic candidate.

The study conducted by Iftikhar *et al.* (2023) evaluated the antihypertensive effects of the *ethyl acetate fraction* (EAF) derived from *Citrullus colocynthis* fruit using a genetic hypertension model, specifically *Spontaneously Hypertensive Rats* (SHR). The fraction was found to contain high levels of flavonoids and polyphenols, including quercetin and myricetin, with a total flavonoid content of 7.6 mg/g, and demonstrated significant antihypertensive effects, as indicated by decreases in systolic, diastolic, and mean arterial pressure (MAP). Furthermore, administration of this fraction improved electrocardiogram patterns and reduced pulse wave velocity (PWV), indicating an improvement in vascular function. These effects are closely associated with the activity of flavonoids, which operate through two principal mechanisms: first, by enhancing the body's antioxidant capacity through normalization of endogenous enzyme levels such as SOD (*superoxide dismutase*) and GSH (*glutathione*), along with reductions in MDA (*malondialdehyde*) and NOx levels, and second by improving vascular elasticity and reducing vascular stiffness. Thus, flavonoids in *C. colocynthis* directly contribute to blood pressure reduction and improvement of hemodynamic function, thereby positioning this fraction as a promising candidate for safe and effective natural antihypertensive therapy.

The study conducted by Araujo-León *et al.* (2024) sought to characterize bioactive metabolites, particularly flavonoids and phenolic acids, present in the leaves and flowers of *Amaranthus cruentus*, and to assess their potential

antihypertensive effects through *in vitro*, *ex vivo*, and *in silico* approaches. Methanolic extracts obtained from the leaves and flowers were analyzed using HPLC-UV-DAD and UV-Vis spectrophotometry for the identification of bioactive constituents, while biological evaluations were conducted to determine *Angiotensin-Converting Enzyme* (ACE) inhibitory activity, rat aortic relaxation, and molecular docking interactions with the ACE enzyme. The findings revealed that *A. cruentus* leaves contained a total flavonoid content of 5.2 mg/g dry weight, comprising compounds such as *quercetin*, *kaempferol*, *catechin*, *hesperetin*, *naringenin*, *hesperidin*, and *naringin*, with *catechin* identified as the predominant constituent. These flavonoids demonstrated pronounced antihypertensive activity, as evidenced by ACE inhibition ranging from 53–58%, approaching the efficacy of captopril, alongside inducing up to 45% aortic relaxation in *ex vivo* experiments. Furthermore, molecular docking analyses revealed that *catechin* exhibits strong binding affinity toward the ACE active site, thereby supporting a direct enzyme inhibitory mechanism. In addition to their effects on ACE, flavonoids in *A. cruentus* also act as potent antioxidants capable of neutralizing free radicals and enhancing *nitric oxide* (NO) bioavailability, which strengthens vasodilatory effects and vascular protection.

The study conducted by Noer *et al.* (2023) reported that the 70% ethanol extract of *Persea americana* Mill. leaves exhibited antihypertensive effects in white rats with NaCl 2% and prednisone-induced hypertension. The flavonoids present in avocado leaves were found to inhibit ACE activity, which prevents the conversion of angiotensin I to angiotensin II, thereby reducing vasoconstriction and lowering blood pressure. The results showed that

doses of 250 mg/kg body weight and 375 mg/kg body weight significantly reduced systolic and diastolic blood pressure and were not significantly different from the positive control captopril, whereas the 125 mg/kg body weight dose still produced a reduction in blood pressure but remained significantly different from the positive control. This activity was also supported by the presence of alkaloids and saponins in avocado leaves, which may contribute to the antihypertensive effect. Thus, this study supports the potential application of avocado leaves as a safe and promising natural alternative for antihypertensive therapy, while further investigations are still needed to isolate specific active compounds and to validate their mechanisms of action in hypertension management.

The study by Uorakkottil *et al.* (2024) explored the antihypertensive potential of eupalitin 3-O- β -D-galactopyranoside, a flavonoid glycoside isolated from the leaves of *Boerhavia diffusa*. This research employed a methylprednisolone-induced hypertensive rat model, in which administration of the active compound resulted in a significant reduction in both systolic and diastolic blood pressure. The primary mechanism proposed involves inhibition of angiotensin-converting enzyme (ACE) activity, as supported by *in silico* findings indicating a strong binding affinity of eupalitin 3-O- β -D-galactopyranoside toward the ACE active site. This antihypertensive effect was further substantiated by *in vivo* results demonstrating statistically significant efficacy ($p < 0.01$), alongside a pharmacokinetic profile suggestive of moderate bioavailability. In addition to its ACE inhibitory activity, this flavonoid also contributes to vascular protection through the attenuation of oxidative stress and enhancement of vascular wall stability.

Through the combined effects of enzymatic inhibition and endothelial protection, eupalitin 3-O- β -D-galactopyranoside from *Boerhavia diffusa* exhibits strong potential as a plant-derived antihypertensive therapeutic candidate acting via modulation of the renin-angiotensin system and oxidative regulation.

Based on the study conducted by Sopian *et al.* (2024), the antihypertensive activity of *Brassica oleracea* (cabbage) leaves was investigated using an *in vivo* experimental model in male Wistar rats, in which hypertension was induced through the combined administration of prednisone and 2.5% NaCl solution. The 96% ethanol extract of *Brassica oleracea* leaves was administered for 14 days at three dose levels (100, 200, and 400 mg/kg body weight), with captopril serving as the positive control. Blood pressure assessment using a non-invasive blood pressure (NIBP) system demonstrated that treatment with the extract at 400 mg/kg body weight resulted in a statistically significant reduction in both systolic and diastolic blood pressure compared with the negative control group ($p < 0.05$). The total flavonoid content in the extract was 8.622 mg QE/g, with quercetin identified as the predominant constituent. Flavonoids in cabbage leaves are proposed to exert vasodilatory effects primarily through inhibition of calcium ion influx into vascular smooth muscle cells, which promotes vascular relaxation and results in reduced peripheral vascular resistance. In addition, flavonoids exhibit antioxidant activity capable of attenuating oxidative stress and preserving endothelial integrity from free radical-induced damage. The combined vasorelaxant and antioxidant properties position cabbage leaf flavonoids, particularly quercetin, as key compounds underlying blood pressure reduction mechanisms, while also reinforcing the

potential of *Brassica oleracea* as a natural antihypertensive agent.

The study conducted by Hess *et al.* (2024) investigated the antihypertensive potential of flavonoids from the leaves of *Psidium guajava* L. using an *in silico* approach involving molecular docking, pharmacophore prediction, and ADMET evaluation. Guava leaves are known to contain flavonoids such as quercetin, kaempferol, luteolin, and chlorogenic acid, which were assessed for their inhibitory activity against *Angiotensin-Converting Enzyme* (ACE). The molecular docking analysis revealed that luteolin and chlorogenic acid demonstrated markedly negative binding energies toward ACE, approaching those of the reference ligand lisinopril, accompanied by lower inhibition constants, indicating strong binding affinity. These interactions occur at key ACE active-site residues, including His353, Glu384, and Tyr523, which are essential in the conversion of angiotensin I to angiotensin II; consequently, ACE inhibition by flavonoids may attenuate vasoconstriction and contribute to blood pressure reduction. In addition, flavonoids in guava leaves exhibit antioxidant activity capable of scavenging free radicals and mitigating oxidative stress in the vascular endothelium, a critical factor in preventing hypertension-induced vascular damage. ADMET profiling demonstrated that the majority of flavonoids adhere to Lipinski's rule, with favorable absorption properties, stable distribution, and low toxicity, substantiating the potential of *P. guajava* flavonoids for development as safe and efficacious antihypertensive phytopharmaceutical agents.

Although the reviewed studies investigated different medicinal plants using various experimental approaches, several consistent antihypertensive mechanisms were identified. ACE

inhibition was the most frequently reported mechanism and was demonstrated in studies involving *Ajuga integrifolia*, *Annona muricata*, *Amaranthus cruentus*, *Boerhavia diffusa*, *Persea americana*, and *Psidium guajava*. In contrast, *Crinum zeylanicum* and *Limonia acidissima* mainly exerted antihypertensive effects through enhancement of nitric oxide bioavailability and endothelial protection, while *Citrullus colocynthis* and *Brassica oleracea* primarily demonstrated antioxidant-mediated vascular protection.

The available evidence also varied considerably according to study design. *In silico* studies provided important preliminary information regarding molecular interactions between flavonoids and ACE; however, these findings require biological confirmation. *In vitro* and *ex vivo* studies further supported the proposed mechanisms, whereas animal studies provided stronger evidence of blood pressure reduction under experimental conditions. Therefore, although all reviewed studies indicate promising antihypertensive potential, the current evidence remains predominantly preclinical and should be interpreted cautiously until supported by clinical trials.

The findings of the present review are consistent with previous reviews on the antihypertensive properties of flavonoids. Maaliki *et al.* (2019) reported that flavonoids exert antihypertensive effects through multiple complementary mechanisms, including inhibition of angiotensin-converting enzyme (ACE), enhancement of endothelial nitric oxide (NO) production, attenuation of oxidative stress, and modulation of inflammatory pathways involved in vascular dysfunction. Similarly, Tabassum and Ahmad (2011) highlighted that medicinal plants rich in flavonoids may contribute to blood pressure reduction through vasodilatory,

antioxidant, and renoprotective effects. The consistency between the findings of the present review and these broader reviews strengthens the biological plausibility of flavonoid-containing medicinal plants as promising candidates for hypertension management. Nevertheless, the current evidence remains predominantly preclinical; therefore, additional pharmacological investigations and well-designed clinical trials are still required to confirm their therapeutic efficacy and safety in humans.

CONCLUSION

Current evidence indicates that flavonoid-containing medicinal plants exhibit promising antihypertensive activity through multiple complementary mechanisms, particularly ACE inhibition, enhancement of nitric oxide bioavailability, antioxidant activity, and improvement of endothelial function. Nevertheless, the available evidence is predominantly derived from *in silico*, *in vitro*, *ex vivo*, and animal studies, which differ in their levels of scientific evidence. Consequently, although these medicinal plants represent promising candidates for future phytopharmaceutical development, further isolation of active flavonoids, pharmacological investigations, toxicity studies, and well-designed clinical trials are required to establish their efficacy and safety in humans.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest associated with this article. This article was conducted and written independently. The authors further confirm that they have no financial or personal affiliations with any individuals or organizations that could have unduly influenced this article.

ACKNOWLEDGEMENT

The authors would like to express their heartfelt gratitude to the supervising lecturers, colleagues, and all individuals who contributed to the preparation of this article. The authors also extend their deep appreciation to Universitas Udayana, particularly the Faculty of Mathematics and Natural Sciences, for providing invaluable facilities and institutional support that greatly facilitated the successful completion of the article.

REFERENCES

1. Adefegha SA, Oyeleye SI, and Oboh G. Distribution of Phenolic Contents, Antidiabetic Potentials, Antihypertensive Properties, and Antioxidative Effects of Soursop (*Annona muricata* L.) Fruit Parts *In vitro*. *Biochemistry Research International*. 2015; 4(2): 1-8.
2. Araujo-Leon JA, Pino IS, Andrade RO, Figueroa SH, Lanestosa AC, Argaez LGB, Sanchez AG, Vallejos GG, Abreu OH, Sanchez SRP, Lopez AX, and Hernandez VA. HPLC-based Metabolomic Analysis and Characterization of *Amaranthus cruentus* Leaf and Inflorescence Extracts for Their Antidiabetic and Antihypertensive Potential. *Molecules*. 2024; 29(3):1-24.
3. Ariani N, Febrianti DR, dan Niah R. Tingkat Pengetahuan Pasien Tentang Efek Samping Obat Captopril dan Amlodipin di Puskesmas Sungai Jingah. *Jurnal Ilmiah Ibnu Sina (JIIS) Ilmu Farmasi dan Kesehatan*. 2020; 5(2):230–239.
4. Fatima S, and Mahmood S. Combating a Silent Killer -The Importance of Self Screening of Blood Pressure From Early Age. *EXCLI Journal*. 2021; 20(1):1326-1327.

5. Hermann M, Flammer A, and Lüscher TF. Nitric Oxide In Hypertension. *Journal of Clinical Hypertension*. 2006; 8(17):17–29.
6. Hess AY, Ramadhani SZ, Andhryanti RN, Zhafirah N, Muljono FO, Fardhan FM, dan Novitasari D. *In silico* Study of Bioactive Compounds in Guava Leaves (*Psidium guajava* L.) Toward Angiotensin Converting Enzyme (ACE) as Target for Hypertension. *Indonesian Journal of Chemical Science*. 2024;13(3):208-219.
7. Iftikhar N, Hussain AI, Fatima T, Alsuwayt B, and Althaiban AK. Bioactivity-Guided Isolation and Antihypertensive Activity of *Citrullus colocynthis* Polyphenols In Rats With Genetic Model of Hypertension. *Medicina*. 2023;59(1880):1-19.
8. Iqbal, A. M. and Jamal, S. F. *Hipertensi Esensial*. StatPearls Publishing. 2023.
9. Kemenkes RI. *Dasar-Dasar Kefarmasian Jilid 1*. Kementrian Kesehatan Republik Indonesia. 2013.
10. Maaliki D, Shaito A, Pintus G, and Eid A. H. Flavonoids In Hypertension: A Brief Review of The Mechanisms And Bioavailability Issues. *Current Opinion in Pharmacology*. 2019; 45: 57–63.
11. Ndjenda IIMK, Mbuyo EPN, Atsamo AD, Fofie CK, Fodem C, Nguemo F, and Nguenefack TB. Antihypertensive Effects of The Methanol Extract and The Ethyl Acetate Fraction From *Crinum zeylanicum* (*Amaryllidaceae*) Leaves In L-Name-Treated Rat. *Evidence-Based Complementary and Alternative Medicine*. 2021; 1-12.
12. Noer SF, Irfayanti NA, dan Rahmat IM. Aktivitas Antihipertensi Ekstrak Etanol Daun Alpukat (*Persea americana* Mill.) pada Tikus Putih (*Rattus norvegicus*). *Media Farmasi*. 2023; 19(2): 87-95.
13. Pertiwi CJP, Muchlisin MA, Jamil AS, Astuti EJ, dan Rafikayanti A. Potensi Kawista (*Limonia acidissima*) dalam Pengelolaan Hipertensi: Analisis Jejaring Farmakologi. *Jurnal Kesehatan Tambusai*. 2024;5(2):4420-4431.
14. Sopian A, Yunarto N, dan Firdaus DA. Uji Antihipertensi Ekstrak Etanol 96% Daun Kubis (*Brassica oleracea* L.) pada Tikus Putih Jantan (*Rattus norvegicus*) Galur Wistar. *Jurnal Ilmiah Farmasi Terapan & Kesehatan*. 2024; 2(2):1-15.
15. Tabassum N and Ahmad F. Role of Natural Herbs in The Treatment of Hypertension. *Pharmacogn Rev*. 2011; 5(9): 30–40.
16. Tessema FB, Gonfa YH, Asfaw TB, Tadesse MG, and Bacheti RK. *In silico* Molecular Docking Approach to Identify Potential Antihypertensive Compounds From *Ajuga integrifolia* Buch-Ham. *Ex D. Don (Armagusa)*. 2024; 17:47-59.
17. Uoorakkottil I, Koottangodan R, Thajudheen KY, Alsheri SA, and Ahmed M. Molecular Docking and Antihypertensive Activity of Eupalitin 3-O-B-D-Galactopyranoside Isolated from *Boerhavia diffusa* Linn. *Pharmaceutics*. 2024; 16(1628): 1-16.