

ANTIHYPERTENSIVE POTENTIAL OF *Anredera cordifolia*: A NARRATIVE REVIEW OF PRECLINICAL AND CLINICAL EVIDENCE

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Received: 30/07/2026 Revised: 25/09/2026 Accepted: 29/09/2026 Published: 01/10/2026

ABSTRACT

Hypertension is a condition that develops gradually but can suddenly lead to serious consequences, including death. The use of natural ingredients as adjunctive therapy continues to grow, including *Anredera cordifolia*, more commonly known as the binahong plant. Ethanol extracts of *A. cordifolia* leaves are known to contain vitexin (flavonoids), tannins, saponins, betalains, betanidin (alkaloids), phenols, terpenoids, and ursolic acid. A narrative review was conducted to identify relevant studies published in PubMed, Scopus, and Google Scholar databases between 2016 and 2026. The search terms related to “Anredera” AND “Hypertensive” found 625 articles. Following the screening of titles and abstracts and subsequent full-text assessment based on the predefined inclusion and exclusion criteria, 15 articles were considered eligible and included in the review. The articles consistently demonstrated that *A. cordifolia* leaves exhibit antihypertensive effects *in vitro*, *ex vivo*, *in vivo*, and through empirical use in humans. In humans, it lowers both systolic and diastolic blood pressure. These antihypertensive activities occur through several mechanisms, including inhibition of angiotensin-converting enzyme (ACE), vasodilatory effects via the nitric oxide (NO) pathway, inhibition of angiotensin type 1 receptors and adrenergic receptors, and as a (weak) diuretic. This presents an opportunity to develop traditional medicine as an adjunct to antihypertensive therapy. However, further clinical research is still needed to confirm its efficacy, safety, and optimal dosage for human use. **Keywords:** *Anredera cordifolia*, antihypertensive activity, blood pressure, hypertension, phytochemicals.

INTRODUCTION

Hypertension is frequently referred to as a “silent killer” because it usually has no early symptoms but can hit abruptly. The World Health Organization (WHO) and the

European Society of Cardiology (ESC) define a systolic blood pressure (SBP) of 140 mmHg or higher and/or a diastolic blood pressure (DBP) of 90 mmHg or higher as clinical definitions of hypertension

(WHO, 2025a; McEvoy *et al.*, 2024), whereas, the American College of Cardiology (ACC) and American Heart Association (AHA) categorize stage 1 hypertension as when SBP reaches 130–139 mmHg and DBP of 80–89 mmHg. Moreover, SBP $\geq$ 140 mmHg and DBP $\geq$ 90 mmHg are classified as stage 2 hypertension (Jones *et al.*, 2025).

Hypertension is a comorbid condition that can significantly lead to stroke, myocardial infarction, heart failure, and kidney failure (Iqbal & Jamal, 2023). Approximately 33% of the global population aged 30–79 years suffers from hypertension. Global estimates for 2021 indicate that 53% of deaths are due to cardiovascular diseases (CVDs). The prevalence of hypertension in Asia alone reaches 30% (WHO, 2025b). In 2019, the Eastern Mediterranean region had the highest prevalence (38%), followed by the South-East Asia region (32%) and Western Pacific (29%) (WHO, 2023). According to data from the 2023 Indonesian Health Survey, Indonesia has a prevalence of 8.6% for hypertension among the population aged $\geq$ 18 years out of the total population, while in the 2020 JKN statistical data, hypertension is the condition with the highest number of visits based on secondary diagnoses in Advanced Outpatient Care

(Kemenkes RI, 2023; DJSN BPJS, 2022). Risk factors that can lead to hypertension include advancing age, genetics or family history, an unhealthy lifestyle, the effects of certain medications (e.g., NSAIDs), ethnicity, certain medical conditions (chronic kidney disease, metabolic syndrome, obesity, or thyroid disorders), gender (men are at higher risk than women), and socioeconomic status (NHLBI, 2024).

First-line therapies for hypertension, such as angiotensin-converting enzyme inhibitors (ACEIs), thiazide diuretics, long-acting dihydropyridine calcium channel blockers (CCBs), and angiotensin receptor blockers (ARBs), are strongly recommended to prevent further progression of cardiovascular disease (Jones *et al.*, 2025). Long-term use of these medications regularly brings about unwanted side effects. Specifically, extended therapy with ARBs and ACEIs can cause both hyperkalemia and a decline in kidney function, with ACEIs frequently causing a distinct, ongoing dry cough as well (Ngai *et al.*, 2025). Beyond adverse drug events, the efficacy of antihypertensive therapy is restricted by financial costs, high pill burdens, extended treatment timelines, and insufficient provider counseling regarding medication compliance. Because adherence rates drop as therapeutic regimens grow

more complex and require more medications, sub-optimal compliance presents a major complication in patient care (Flack *et al.*, 2024). This has spurred the search for safer alternatives or adjunct therapies, such as using medicinal plants.

Modern healthcare has recognized the value of medicinal plants, triggered by rising consumer demand for natural, holistic treatments and the urgent need for novel therapies targeting complex diseases. These botanical resources present an ideal framework for creating sustainable, effective, and innovative medical treatments. Furthermore, they offer affordable healthcare alternatives for marginalized communities, support preventive medicine initiatives, and encourage collaborative research across diverse scientific disciplines (Hossain *et al.*, 2024).

The *Anredera* genus, particularly *Anredera cordifolia* (Figure 1), has drawn significant attention for its antihypertensive properties. Ethanolic leaf extracts of *A. cordifolia* are rich in bioactive compounds, including flavonoids, phenols, alkaloids, steroids, and saponins (Dwitiyanti *et al.*, 2019a). Medicinal plants high in phenols and flavonoids are inversely linked to CVDs and hypertension risks (Grosso *et al.*, 2022;

Wan *et al.*, 2024), though these effects differ markedly by age and metabolic status (Niu *et al.*, 2025).

However, existing data on *A. cordifolia* are highly fragmented due to different extraction methods, experimental models, dosages, and treatment periods across studies. To date, no single review has integrated *in vitro*, *ex vivo*, and *in vivo* findings to map out a clear pharmacological framework or connect specific phytoconstituents to their mechanism of action. Consequently, this study compiles scientific data on the blood-pressure-lowering activity of *A. cordifolia* leaves to support its application as a complementary hypertension treatment. Specifically, this review aims to synthesize available preclinical and clinical evidence regarding its efficacy; map out its underlying pharmacological mechanisms; evaluate its safety profile, tolerability, and herb-drug interactions with standard therapies; and highlight current knowledge gaps to guide future research toward clinical translation.



Figure 1. *Anredera cordifolia*
[Source : personal document]

METHODS

A comprehensive literature search was conducted in April 2026 across three electronic databases: PubMed, Scopus, and Google Scholar, to identify relevant studies published between 2016 and 2026. The search strategy employed combinations of medical subject headings (MeSH) and keywords utilizing Boolean operators, specifically: "Anredera" AND "Hypertensive". This initial search retrieved 625 articles (PubMed: n = 1; Scopus: n = 4; Google Scholar: n = 620).

Following the initial retrieval, duplicates were removed, and the remaining records were screened against strict eligibility criteria (Figure 2). Studies were included if they: (1) evaluated the antihypertensive or cardiovascular effects of *Anredera cordifolia*, administered either as

a monotherapy or in combination with other botanical extracts; (2) were original research articles featuring complete experimental designs and full-text results; and (3) were published in either English or Indonesian. Conversely, publications were excluded if they lacked relevance to blood pressure or cardiovascular physiology, did not explicitly investigate *A. cordifolia*, or lacked sufficient quantitative or qualitative data for robust extraction.

A structured narrative synthesis was adopted to systematically analyze and critically interpret the compiled evidence. To ensure a rigorous synthesis, findings were categorized by study type (*in vitro*, *in vivo*, *ex vivo*, and clinical trials). The analysis systematically accounted for variations in extract characteristics, experimental models, dosage regimens,

primary outcomes, and proposed molecular mechanisms.

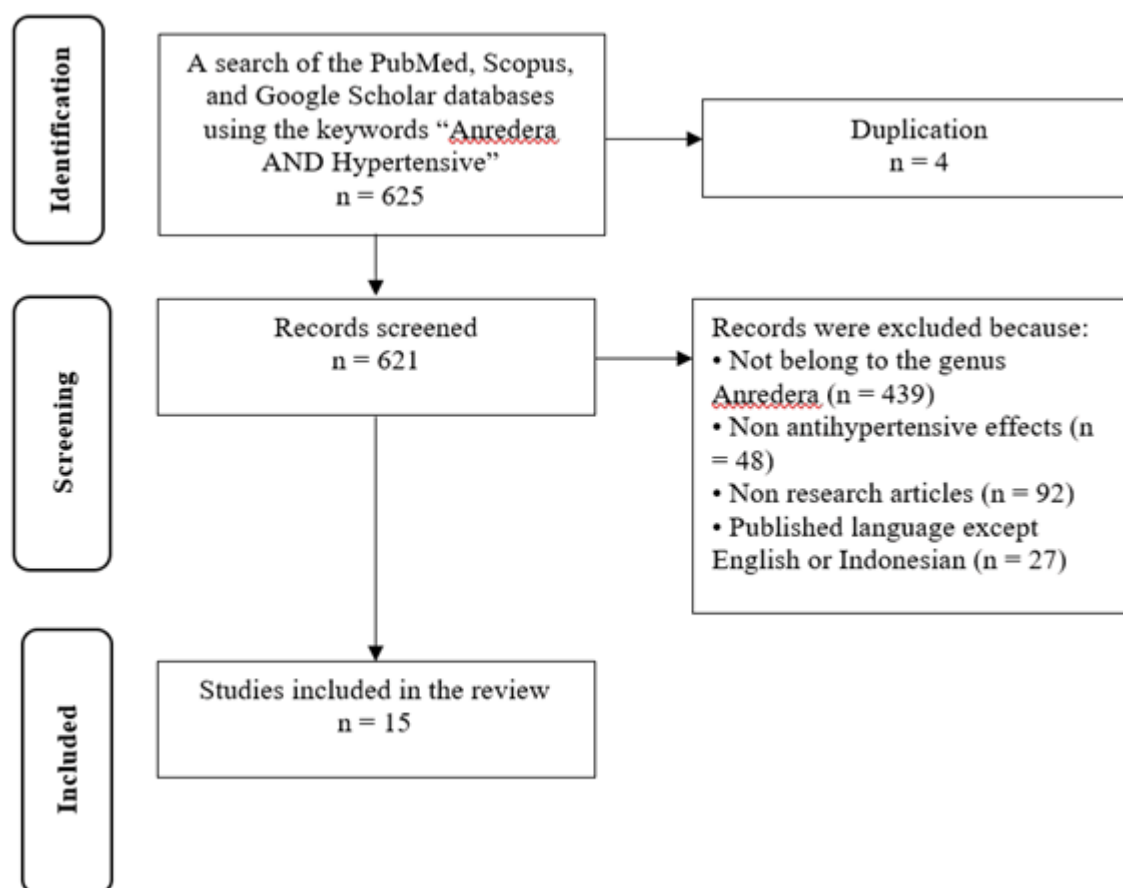


Figure 2. The literature search flowchart (n = number of articles)

RESULT & DISCUSSION

Fifteen articles have reported the antihypertensive activities of *A. cordifolia*. The leaf has been the most studied and has demonstrated consistent antihypertensive effects, as evidenced by *in vitro* testing, animal studies (*in vivo* and *ex vivo*), and empirical human studies, summarized in Table 1. Ethanol was the commonly used solvent for extraction, as reported in 7

articles. Studies were conducted primarily in Indonesia.

1. Botanical Aspects of *A. cordifolia*

A. cordifolia (Ten.) Steenis or its synonyms *Boussingaultia gracilis*, *Boussingaultia cordifolia*, and *Boussingaultia cordata*, originally came from China under the name *Dheng Shan Chi* before spreading to Southeast Asia. In England, this plant is called the Madeira vine or Mignonette vine (Sidhartha *et al.*,

2024). In Indonesia, it is referred to as binahong, piahong, or sirih raja (Hasbullah, 2016). The most widely utilized part of this plant is the leaves. Tannins (0.2512% w/w), flavonoids (0.2433% w/w), saponins (0.1631%), and alkaloids (0.0350%) are the secondary metabolites of the ethanolic extract of *A. cordifolia* leaves (Tandi *et al.*, 2023). The total flavonoid content (as rutin) of the ethanol extract of leaves was 48.3 mg RE/100 g of extract, and the total phenolic content (as gallic acid) was 22.376 g GAE/100 g of extract (Herawati *et al.*, 2025).

2. Toxicity Studies of *A. cordifolia* Extracts

The safety of *A. cordifolia* extract was investigated in acute toxicity, 28-day sub-chronic toxicity, and teratogenicity studies, as follows:

In an acute toxicity study carried out in Banda Aceh, Indonesia, the ethanol extracts of *A. cordifolia* leaves at doses ranging from 300 to 2400 mg/kg body weight did not cause death in experimental male Wistar rats. There was a decrease in locomotor activity in groups given doses of 1200 and 2400 mg/kg body weight. Overall, no significant toxic effects, as measured by liver histology and body weight, were found, suggesting the safety of the extracts,

with an LD₅₀ greater than 2400 mg/kg body weight (Suryawati *et al.*, 2022).

In another study carried out in Bali, Indonesia, *A. cordifolia* leaf extract was investigated in mice at fixed doses of 5, 50, 300, 2000, and 5000 mg/kg body weight for an acute toxicity test, and at 250, 500, and 1000 mg/kg body weight for a 28-day sub-chronic toxicity test. It was concluded that the extract was categorized as practically not toxic, with an LD₅₀ greater than 5000 mg/kg body weight; however, there were slight abnormalities in liver and kidney function at doses of 500 and 1000 mg/kg body weight, as shown by the increase in SGOT, BUN, and serum creatinine levels (Lesmana *et al.*, 2022).

The teratogenicity effects of the ethanol extract of *A. cordifolia* leaves at doses of 100, 400, and 1000 mg/kg body weight were also assessed in Wistar rats. Evaluation was done on the fetal skeleton, organs, and fetal weight, and revealed that doses of 100, 400, and 1000 mg/kg body weight did not cause teratogenic effects (Sukandar *et al.*, 2014).

The effects of *A. cordifolia* leaf extract were also studied on the liver of guinea pigs (*Cavia cobaya*). This study revealed that the leaf extracts up to the dose of 90 mg/head did not cause significant toxicity effects on the liver of

guinea pigs, thus confirming their safety (Wijayanti *et al.*, 2019).

3. Antihypertensive Effects of *A. cordifolia* Extracts

Across the included studies, *A. cordifolia* extracts were generally investigated for their antihypertensive effects by *in vitro* testing in one article and animal studies (*in vivo* and *ex vivo*) in 8 articles. The inducers used were variable, such as dexamethasone (at a dose of 0.5 mg/kg body weight for 10 days or 14 days),

epinephrine (at a dose of 0.25 mg/kg body weight or 1.2 mg/kg body weight intraperitoneally), angiotensin II (at a dose of 0.25 mg/kg body weight or 1.2 mg/kg body weight intraperitoneally), and high-fat diet. The doses of *A. cordifolia* extracts also varied from 50, 100, 200, 300, and 400 mg/kg body weight for single form, and 25 mg/kg body weight when combined with other plant extract.

The results were summarized in Table 1 for the *in vitro* testing and animal studies.

Table 1. Studies on the antihypertensive effects of *a. cordifolia* *in vitro*, *in vivo*, and *ex vivo*

Methods	Dose of <i>A. cordifolia</i> and control	Mechanism of Action	Result	Ref.
<i>In vitro</i> studies				
The inhibitory effects on ACE activity were investigated using Hip-His-Leu as the substrate and the product was measured at 228 nm.	The ethanolic extract, hexane fraction, ethyl acetate fraction, and water fraction of AC were tested at concentrations of 6.25, 12.5, 25, 50, and 100 µg/mL	Not investigated	IC ₅₀ for the ethanolic extract, hexane fraction, ethyl acetate fraction, and water fraction were 22.63 µg/mL, 242.60 µg/mL, 115.77 µg/mL, and 97.53 µg/mL, respectively.	(Garmana <i>et al.</i> , 2017)
<i>In vivo</i> studies				
Dexamethason e- induced hypertension in Wistar rats	1. ACLE 100 mg/kg body weight 2. 0.02 mg/kg body weight of n-hexane fraction 3. 1.66 mg/kg body weight of ethyl acetate	Vasodilation effect through the NO pathway and antioxidant properties.	The ethyl acetate and water fractions have significant antihypertensive effects.	(Garmana <i>et al.</i> , 2018)

Methods	Dose of <i>A. cordifolia</i> and control	Mechanism of Action	Result	Ref.
	fraction. 4. 40.73 mg/kg body weight of water fraction. 5. The positive control group was given 0.45 mg/kg body weight of amlodipine. Extract, fractions, and amlodipine were administered on days 8–14. Dexamethasone 0.5 mg/kg body weight was administered on days 1–14 to induce hypertension.			
Epinephrine-induced hypertension in Wistar rats	For acute antihypertensive effect: ACLE was tested at doses of 50, 100, and 200 mg/kg body weight. The standard for antihypertensive effect was atenolol 9 mg/kg body weight. Epinephrine or adrenaline 1.2 µg/kg body weight was used to induce hypertension. For diuretic effect: The extract was tested at the same doses. The standard for diuretic effect was furosemide 20 mg/kg body weight.	β-adrenergic receptor antagonists and diuretic effect.	ACLE dose of 50 mg/kg body weight had significant antihypertensive activity but showed weak diuretic effect.	(Garmana <i>et al.</i> , 2016)
Epinephrine-induced hypertension	1. Hypertensive rat without treatment 2. ACLE 50 mg/kg body weight	Inhibition of adrenergic receptor	50–50 mg/kg body weight combination of ACLE and SA	(Suliska <i>et al.</i> , 2021)

Methods	Dose of <i>A. cordifolia</i> and control	Mechanism of Action	Result	Ref.
in Wistar rats	3. ACLE 100 mg/kg body weight 4. SA 50 mg/kg body weight 5. SA 100 mg/kg body weight 6. ACLE 25 mg/kg body weight + SA 25 mg/kg body weight, and 7. ACLE 50 mg/kg body weight + SA 50 mg/kg body weight 8. Atenolol 4.5 mg/kg body weight. Epinephrine 0.25 mg/kg body weight intraperitoneally was used to induce hypertension. AC was extracted with 70% ethanol, and SA was extracted with water.		extract showed the best effect in lowering blood pressure	
Dexamethason e-induced hypertension in Wistar rats	1. Normal group 2. Control group 3. Captopril 13.5 mg/kg body weight 4. SA 25 mg/kg body weight and AC 25 mg/kg body weight 5. SA 50 mg/kg body weight and AC 50 mg/kg body weight 6. SA 50 mg/kg body weight and AC 50 mg/kg body weight 7. SA 100 mg/kg body weight 8. AC 100 mg/kg body weight Dexamethasone 0.5 mg/kg body weight	AC increases NO levels, whereas SA is known to inhibit ACE	50–50 mg/kg body weight combination of SA and AC extracts showed the greatest reduction in BP compared to other groups.	(Sukandar <i>et al.</i> , 2023)

Methods	Dose of <i>A. cordifolia</i> and control	Mechanism of Action	Result	Ref.
	was administered intraperitoneally on days 1–10 to induce hypertension. The aqueous extracts were given orally every day for seven days after dexamethasone induction.			
Angiotensin II-induced hypertension in Wistar rats	1. ACLE 50 mg/kg body weight 2. ACLE 100 mg/kg body weight 3. SALE 50 mg/kg body weight 4. SALE 100 mg/kg body weight 5. ACLE-SALE combination (25-25 mg/kg body weight) 6. ACLE-SALE combination (50-50 mg/kg body weight) 7. Valsartan 7.2 mg/kg body weight 8. Positive control 9. Normal/negative control	Antagonist effect against angiotensin II on AT1 receptor.	A combination of ACLE-SALE (25-25 mg/kg body weight) was the most effective dose.	(Sukandar <i>et al.</i> , 2019)
HFD-induced hypertension in Wistar rats for 14 days.	Normal control, ACLE treatment dose 200 mg/kg body weight, 300 mg/kg body weight, and 400 mg/kg body weight for two weeks after induction.	Lowering TC, TG, LDL-C levels and increasing HDL-C levels and inhibiting the formation of foam cells.	Dose of 400 mg/kg body weight effectively reduced the thickness of the aortic wall and the number of aortic foam cells in rats.	(Wahyudi <i>et al.</i> , 2023)

Methods	Dose of <i>A. cordifolia</i> and control	Mechanism of Action	Result	Ref.
<i>Ex Vivo</i> studies				
NE and potassium chloride pre-contracted the rabbit aorta rings, and NE pre-contracted the frog heart	NE and potassium chloride pre-contracted the rabbit aorta rings: 1. ACLE (0.9 mg/mL), Ethanolic 2. Extract of SA leaves (0.9 mg/ml) 3. Ursolic acid (0.5 µg/mL) 4. Doxazosin (4.5 µg/mL) 5. Nifedipine (9 µg/mL). NE pre-contracted the frog heart: 1. ACLE (0.9 mg/ml) 2. Ursolic acid (0.5µg/ml) 3. Bisoprolol (2.5µg/ml)	AC has vasodilation effect in rabbit aortic rings (NO pathway) and frog heart, mediated by β 1-adrenoreceptor inhibition.	ACLE produced significant vasodilation of rabbit aorta rings and frog heart.	(Sukandar <i>et al.</i> , 2016)
Rabbit aortas treated with NE, methylene blue-NE, and potassium chloride	ACLE (1.57 mg/mL), water fraction (0.64 mg/mL), ethyl acetate fraction (0.03 mg/mL), and n-hexane fraction (0.004 mg/mL). Terazosin (1.41 µg/mL) was used as a control.	Inhibition of adrenergic receptors, inhibition of calcium ion influx, or vasodilation through NO pathway.	Vasodilatory effects of ACLE are weak.	(Garmana <i>et al.</i> , 2017)

Abbreviations (in alphabetical order): AC, *Anredera cordifolia*; ACE, angiotensin-converting enzyme; ACLE, *Anredera cordifolia* leaves ethanolic extract; AT1, angiotensin 1; HDL-C, high-density lipoprotein cholesterol; HFD, high-fat diet; LDL-C, low-density lipoprotein cholesterol; NE, norepinephrine; NO, nitric oxide; SA, *Sonchus arvensis*; SALE, *Sonchus arvensis* leaves ethanolic extract; TC, total cholesterol; TG, triglycerides

Studies on the antihypertensive effects of *A. cordifolia* in humans are limited, in fact, during this time period, there are only 7 articles (Table 2), with only small sample

size, ranging from 16 to 64 participants, and decoction of the leaves as the most reported preparation. Intriguingly, all studies revealed that consumption of *A. cordifolia*

leaves, regardless of the preparation, resulted in lower blood pressure effects.

Table 2. Studies on the antihypertensive effects of *a. cordifolia* in humans

Methods, characteristics of participants, and study location	Dose of <i>A. cordifolia</i> leaves	Mechanism of Action	Results	Ref
Studies in Humans				
Quasi-comparative experiment recruiting 64 participants with hypertension in Bangkalan and Gresik, East Java.	3 g/200 mL of red ginger rhizome infusion (S1, n = 32) compared with 3 g/200 mL of AC leaf infusion (S2, n = 32) after 4 hours administration in a day.	Prevent ACE activity and decrease oxidative stress.	Both groups showed a lowering of BP.	(Fickri <i>et al.</i> , 2021)
Quasi-comparative experiment recruiting 16 participants with hypertension in Lubuk Buaya.	30 g/600 mL of leaves decoction, twice daily for 7 days.	Reduction of renin production.	The decoction showed a lowering of BP	(Ibrahim <i>et al.</i> , 2019)
Quasi-comparative experiment recruiting 32 participants with hypertension in Pekanbaru.	Decoction of leaves, twice daily for 3 days.	Relaxing smooth muscles.	The decoction showed a lowering of BP	(Firdaus & Rezeki, 2020)
Quasi-comparative experiment recruiting 60 participants with hypertension in Medan.	Decoction of leaves for 7 days.	Relaxing smooth muscles.	The decoction showed a lowering of BP	(Sari, 2022)

Methods, characteristics of participants, and study location	Dose of <i>A. cordifolia</i> leaves	Mechanism of Action	Results	Ref
Quasi-comparative experiment recruiting 27 participants with hypertension in Cilacap, Central Java.	Not described	Inhibition of ACE and diuretic effects.	The decoction showed a lowering of BP	(Wijayanti <i>et al.</i> , 2023)
Quasi-comparative experiment recruiting 44 participants with hypertension in Sleman, Special Regency of Yogyakarta.	The participants were given AC pudding and received acupressure in the morning for 7 days.	Inhibition of ACE	The combination of AC and acupressure could lower BP.	(Asmarani, 2021)
Quasi-comparative experiment recruiting 20 participants with hypertension in Tegalsari village, Gresik, East Java.	30 g/600 mL leaves decoction mixed with 70 mL of honey, twice daily for 7 days.	Relaxing smooth muscle.	The combination of AC and honey could lower BP.	(Wijayanti <i>et al.</i> , 2024)

Abbreviations (in alphabetical order): AC, *Anredera cordifolia*; ACE, angiotensin-converting enzyme; BP, blood pressure.

4. Mechanism of Action of the Phytochemicals

Vitexin (flavonoids), tannins, saponins, betalain (pigments), bethanidine (alkaloids), phenols, terpenoids, and ursolic acid (carboxylic acids) were found in *A. cordifolia* leaves extracted using 96% ethanol (Dwitiyanti *et al.*, 2019a; Ilmiyah *et*

al., 2025). These metabolites have been described for their benefits in maintaining blood pressure, as follows vitexin has been reported to significantly lower systolic and diastolic blood pressures and ameliorate histopathological changes in hypertensive nephropathy (HN) rats (Duan *et al.*, 2024). The ethanolic extract of *A. cordifolia* was

reported to contain a total flavonoid content of 165.34 ± 1.73 μg vitexin equivalents (VE)/mg extract (Suliska *et al.*, 2021). Vitexin exhibits vasodilator activity and reverses the vasoconstrictor response of isolated pulmonary artery to potassium chloride and phenylephrine (Al-Jeboory *et al.*, 2021). When the extract is taken orally, the active ingredients in the extract go through a lot of metabolism in the first pass. The first-pass effects of vitexin in rats were found to be 5.2% in the liver, 31.3% in the stomach, and 94.1% in the intestine (Xue *et al.*, 2021). Other flavonoids such as luteolin, quercetin, and rutin exhibit high ACE-inhibitory activity (Zielińska *et al.*, 2025). Tannins are also known to inhibit ACE non competitively (Liu *et al.*, 2003). Saponins exhibit a protective effect on the kidneys by inhibiting the renin system within the renin-angiotensin-aldosterone system (RAAS) (Chen *et al.*, 2013). Moreover, betalain, an antioxidant pigment, has shown perquisites in controlling blood pressure, which may be related to its high nitrate content (Grönroos *et al.*, 2024). Interestingly, bethanidine was described to be widely used as a third drug combined with a thiazide and a beta blocker to enhance antihypertensive effects (McInnes, 2007). Phenolic acids also have a protective effect on endothelial cells against oxidative damage caused by H_2O_2 by

regulating levels of nitric oxide, glutathione, malondialdehyde, and reactive oxygen species (Yu *et al.*, 2022). Ursolic acid is a pentacyclic triterpene carboxylic acid that has been shown to play important roles in reducing fat accumulation, oxidative stress, obesity, and inflammation, which are responsible for the development of cardiovascular diseases. However, these effects are not significant (Rafiee *et al.*, 2024).

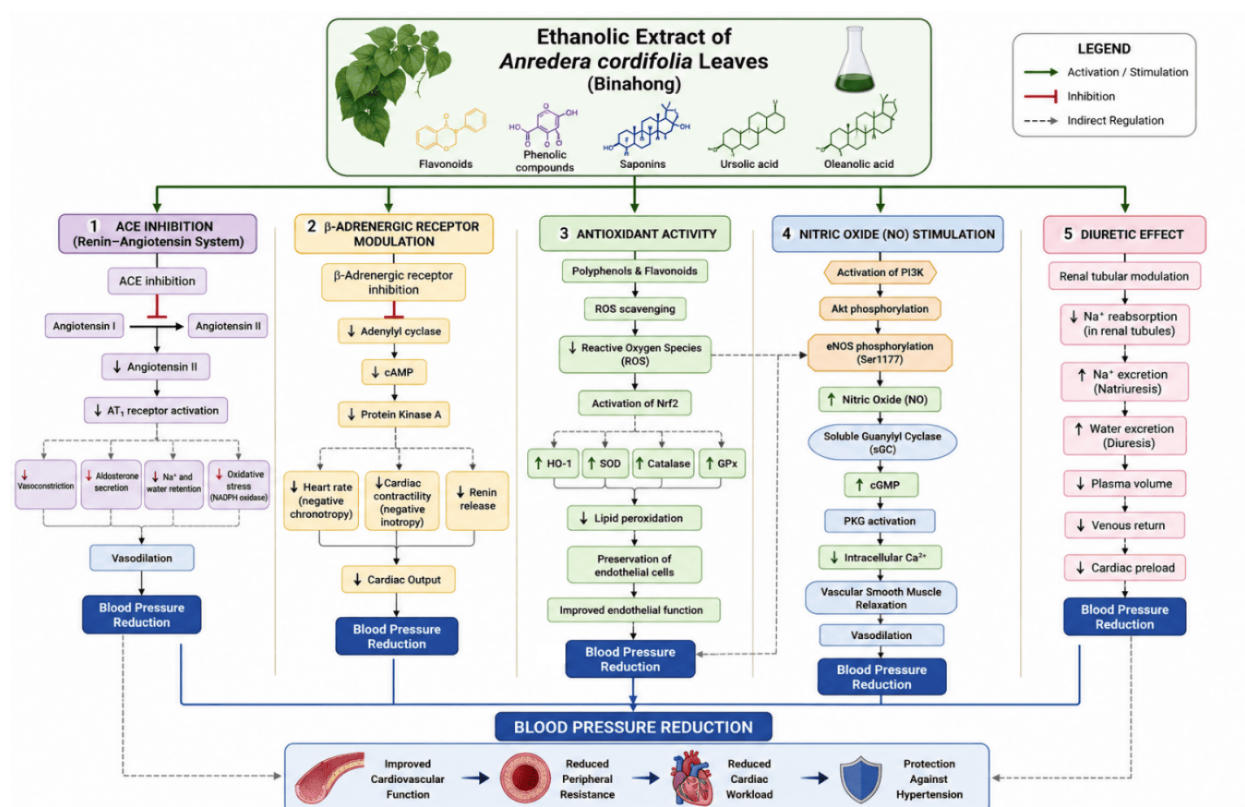


Figure 3. Mechanism of the multitargeted pathway of *a.cordifolia* ethanol extract constituents. [Generated by ChatGPT]

Abbreviations (in alphabetical order): ACE, angiotensin-converting enzyme; AT1, angiotensin II receptor type 1; cAMP, cyclic adenosine monophosphate; cGMP, cyclic guanosine monophosphate; GPx, glutathione peroxidase; HO-1, Heme oxygenase-1; SOD, superoxide dismutase; PKG, cGMP-dependent protein kinase.

5. Herb-Drug Interaction

Ethanol extract of *A. cordifolia* has interaction between the other drugs. The interaction involves cytochrome P450 (CYPs). CYPs are a wide range of proteins that contain heme and a thiolate group, and they can be found in nearly every type of living organism. Out of the 57 human P450 enzymes, the 3A4 form, known as CYP3A4, is the most common and the most significant because it helps break down the majority of the drugs that are taken. It is mostly found in the liver and the digestive system

(Sevrioukova & Poulos, 2013). Vitexin inhibits CYP3A4 and may help make glibenclamide work better as a diabetes medicine (Dwitiyanti *et al.*, 2019b). *A. cordifolia* extract can also help carry antibiotics better, which makes azithromycin more effective in being absorbed into the body. In short, using *A. cordifolia* leaf extract to modify chitosan nanoparticles helped improve how well azithromycin is enclosed and how much of it can be carried by the nanoparticles (Yuniarti & Yulizar, 2023). Following the

discussion of the molecular mechanisms and pharmacological interactions, it is equally important to consider the translational relevance of these findings by converting the effective experimental dose into a human equivalent dose (HED). According to the FDA guidelines for converting doses using body surface area, a dose of 50 mg extract/kg body weight in rats is roughly equivalent to a human dose of about 9.5 mg/kg body weight (Nair & Jacob, 2016).

CONCLUSIONS

A. cordifolia leaves have been shown to have antihypertensive effects based on research findings, particularly from *in vitro*, *in vivo*, and *ex vivo* studies, as well as empirical use in humans. Overall, preclinical findings suggest that *A. cordifolia* has antihypertensive potential, but its therapeutic relevance in humans remains uncertain owing to the limited clinical evidence and methodological limitations of available studies. This suggests that *A. cordifolia* has potential as a complementary therapy for the treatment of hypertension. Limitations of this study include the lack of a standardized dose for hypertension in humans, variations in extraction methods, and the absence of compounds directly isolated from the plant parts. This necessitates further clinical,

standardized, and evidence-based research to support its use in the medical field. Future research should prioritize randomized controlled clinical trials using standardized *A. cordifolia* extracts with defined marker compounds to ensure consistency and reproducibility. Dose-ranging, pharmacokinetic, long-term toxicity, and herb–drug interaction studies are needed to establish appropriate dosing, safety, and clinical applicability. Comparative clinical studies with standard antihypertensive therapy should be conducted, with SBP and DBP defined as primary outcomes. Importantly, the human-equivalent dose (HED) derived from animal studies should be regarded only as a preliminary translational estimate and must not be interpreted as a clinically recommended human dose. Clinical dosing should be established through well-designed human dose-finding studies.

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