



## Review Article

### PLANTS WITH ANTIHYPERTENSIVE ACTIVITIES: A REVIEW

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#### ABSTRACT

Hypertension is one of the most common causes of morbidity and premature death worldwide. Hypertension or high blood pressure is a condition of an increase in systolic blood pressure  $\geq 140$  mmHg and diastolic blood pressure  $\geq 90$  mmHg. Hypertension is very dangerous because in most cases there are no symptoms in the sufferer (silent killer). Conventional treatment for hypertension often causes various side effects, so that the choice of herbal treatment is being considered more. Medicinal plants such as *Cratoxylum formosum*, *Adansonia digitata* L., *Vitex pubescens*, *Cinnamomum zeylanicum*, *Catharanthus roseus*, *Crotalaria burhia*, *Leersia hexandra*, *Moringa oleifera* L., *Allanblackia floribunda*, *Holarrhena floribunda*, *Berberis vulgaris*, *Morinda citrifolia* L., *Ficus carica*, *Bidens pilosa*, *Panax ginseng*, *Lantana camara*, *Allium sativum*, *Apium graveolens*, *Vitex cienkowskii*, and *Achillea wilhelmsii* have antihypertensive activity which can be used as an alternative in the treatment and prevention of hypertension. This review article used the literature study method of national and international journals published in the last 10 years (2010-2020) that was done through several websites such as ScienceDirect, NCBI, ResearchGate and Google Scholar.

**Keywords:** hypertension, silent killer, medicinal plants

#### INTRODUCTION

Hypertension is one of the most common causes of morbidity and premature death worldwide. WHO (World Health Organization) stated that hypertension attacks 22% of the world's population, and 36% of the incidences occurred in Southeast Asia. Hypertension is also a cause of death with 23.7% of the total 1.7 million deaths in Indonesia in 2016<sup>1</sup>. The prevalence of hypertension in Indonesia in 2018 reached 34.1%. This showed an increase where the incidence of hypertension in 2013 was only 25.8%<sup>2</sup>.

Hypertension or what is often called as the silent killer is very dangerous because in most cases there are no symptoms in the sufferer and is the most significant risk factor for atherosclerosis and the clinical manifestations of atherosclerosis include: heart failure, coronary artery disease, stroke, kidney disease, and peripheral artery disease<sup>3</sup>.

Definition of hypertension or high blood pressure is an increase in systolic blood pressure of more than 140 mmHg and diastolic blood pressure of more than 90 mmHg at two measurements with an interval of five minutes in a state of rest / calm. Increased blood pressure that lasts for a long time (persistent) can cause damage to the kidneys (kidney failure), heart (coronary heart disease) and brain (causing stroke) if not detected early and receive adequate treatment<sup>4</sup>.

Treatment for hypertension can be carried out conventionally or herbal. As many as 56% of hypertension sufferers also use herbal

remedies in addition to conventional medicines. The cost of using natural medicines that are considered cheaper and with fewer side effects causes herbal treatment for hypertension to have increased in the last decade<sup>5</sup>.

Antihypertensive drugs have many side effects such as coughing, dizziness, diarrhea, constipation, feeling tired, headache, nausea and weight loss or gain<sup>6</sup>. Therefore, herbal medicine is an alternative that needs to be considered. Herbal medicines that can reduce the risk of hypertension are mostly sourced from plants that grow in various parts of the world. Based on the large number of herbal medicines that have been researched previously, this study will conduct a review of 20 articles about plants that have antihypertensive activity. Thus, one would see the content and the working mechanism of these plants in lowering blood pressure and reducing the risk of hypertension.

#### DATA COLLECTION

In compiling this review article, the technique used was to use the literature study method in the form of national and international journals published in the last 10 years (2010-2020). The search for data on online media was done with the following keywords: Hypertension; Antihypertensives; Herbal plant; and Hypotensive Effects. The search for the main references in this review was carried out through the web such as through ScienceDirect, NCBI, ResearchGate, Google Scholar, and other relevant journal databases.

**Table 1. Plants with antihypertensive activity**

Name of Plant	Part of Plant	Solvent	Extraction Method	Chemical Content	Testing Methods	Antihypertensive Mechanism	Reference
<i>Cratogeomys formosum</i>	Leaves	Water	Infusion	Flavonoids	Animal Testing (Rats)	Increase NO bioavailability and inhibit the effects of the Renin-Angiotensin System (RAS)	7
<i>Adansonia digitata</i> L.	Leather Trunk	Water	Maceration	Antioxidants	Animal Testing (Rats)	Prevent cell damage caused by oxidative stress as well as increasing levels of NO	8
<i>Vitex Pubescens</i>	Leaves	Petroleum Ether, chloroform, methanol, water	Maceration	Spathulenol	Animal Testing (Rats)	Vasorelaxation, Anti-inflammatory, Antimicrobials and Antioxidants	9
<i>Cinnamomum zeylanicum</i>	Tree Bark	-	-	Polyphenols, Coumarin, Cinnamic Acid, Eugenol, and Cinnamaldehyde	Human Subjects	Vasorelaxation effects and reduces systemic vascular resistance	10
<i>Catharanthus roseus</i>	Leaves	Water	Infusion	Alkaloid	Animal Testing (Rats)	Increase antioxidants of endogenous enzyme and suppress the formation of free radicals	11
<i>Crotalaria burhia</i>	All parts of the plant	Water-Methanol	Maceration	Glycosides, Alkaloids, Flavonoids, Quercetin, Saponins, Steroids, and B-Sitosterol	Animal Testing (Rabbit)	Depressant effect, vasodilator, cardio-depressant, blocking calcium channel and diuretic action.	12
<i>Leersia hexandra</i>	Leaves and Stems	Water	Infusion	Antioxidant	Animal Testing (Rats)	Prevents cell damage due to oxidative stress and inhibits lipid peroxidation.	13
<i>Moringa oleifera</i> L.	Leaves	Methanol-Ethyl Acetate	Maceration	Glycosides and Flavonoid	Animal Testing (Rats)	Inhibit or to simpatis and decrease oxidative stress	14
<i>Allanblackia floribunda</i>	Stems	Water	Infusion	Antioxidants (flavonoids)	Animal Testing (Rats)	Reducing arterial blood pressure and increase the oxidative balance.	15
<i>Holarrhena floribunda</i>	Skin Stem and Leaf	Water-Ethanol	Infusion and Maceration	Antioxidants	Animal Testing (Rabbit)	Decrease in vascular permeability and increase capillary resistance	16
<i>Berberis vulgaris</i>	Skin Roots	Water	Infusion	Alkaloids	Animal Testing (Rats)	Inhibits resistance of peripheral vascular	17
<i>Morinda citrifolia</i> L.	Leaves and Fruits	Ethanol	Maceration	Flavonoid, Rutine, and Scopoletin	Animal Testing (Rats)	Prevents cell damage due to oxidative stress and inhibits lipid peroxidation	18
<i>Ficus carica</i>	Fruit	Water-Methanol	Maceration	(Polyphenols) Quercetin, Gallic Acid, Caffeic, Vanillic Acid, Syringic Acid, Coumaric Acid and Chromotropic Acid.	Animal Testing (Rats)	Antioxidant and vasorelaxant effect of blood vessels	19
<i>Bidens pilosa</i>	Leaves	Ethylene acetate	Maceration	Quercetin 3,3 '-dimethyl ether 7 - 0- $\beta$ - D- glucopyranoside.	Animal Testing (Rats)	Vasodilator, inhibits calcium and free radicals that eliminate insulin sensibility, and increases lipid profile	20
<i>Panax ginseng</i>	Root	Ethanol	Reflux	Saponin and Ginsenoside Rg3	Animal Testing (Rats)	Inhibits ACE	21
<i>Lantana camara</i>	Leaves	Ethanol	Soxhlation	Alkaloids, Glycosides, Polypeptides, Saponins	Animal Testing (Rats)	Maintain ionic levels (increase potassium and decrease sodium levels)	22
<i>Allium sativum</i>	Bulb	-	-	-Glutamyl-S-Allyl-Cysteine (GSAC)	Human Subjects	Inhibit ACE	23
<i>Apium graveolens</i>	Seed	Hexane, Methanol, Water-Ethanol	Maceration	N-Butylphthalide (NBP)	Animal Testing (Rats)	Vascular vasodilation effect	24

<i>Vitex cienkowskii</i>	Skin	Methanol	Maceration	Flavonoid, Penta-Cyclic Triterpenoid, and Ceramide	Animal Testing (Rats)	Provides a cardioprotective effect	25
<i>Achillea wilhelmsii</i>	All Parts of the Plant (Except Roots)	Water-Ethanol	Maceration	Alkaloid	Animal Testing (Rabbit)	Vasorelaxant effect on fur blood h	26

***Cratoxylum formosum***



Figure 1. *Cratoxylum formosum*<sup>27</sup>

*Cratoxylum formosum* is a traditional plant and is widely consumed in Thailand. The fresh young leaves of this plant are widely consumed as a vegetable side dish or as an ingredient in food<sup>28</sup>. *Cratoxylum formosum* extract contains high levels of flavonoids, myricetin, luteolin, as well as phenolic acids, syringic acid, protocatechuic acid and vanillic acid<sup>29</sup>. Extracts of *Cratoxylum formosum* demonstrated antioxidant capacity, hemodynamic improvement and vasorelaxant<sup>30</sup>.

Aqueous extract of *Cratoxylum formosum* was proven to have antihypertensive activity tested on L-NAME induced male Sprague-Dawley Rats<sup>7</sup>. Extracts at doses of 100, 300, and 500 mg/kg were significantly able to reduce blood pressure, where the extract at a dose of 300 mg/kg was the effective concentration for lowering blood pressure in hypertensive Rats ( $117.0 \pm 1.9$  mmHg). *Cratoxylum formosum* increased contractile response mediated by the nervous system, as well as increasing the concentration of nitric oxide metabolites (NOx).

***Adansonia digitata* L.**



Figure 2. *Adansonia digitata* L.<sup>31</sup>

*Adansonia digitata* L. is a medicinal plant from the Malvalesorder (family of Bombaceae), which is commonly used in traditional African medicine for cardiovascular disorders<sup>32</sup>. This herb is reported to have anti-inflammatory, antioxidant, antimalarial, and antimicrobial properties<sup>33</sup>. Aqueous extract of *Adansonia digitata* L. was shown to have antihypertensive activity tested on hypertensive male Wistar Rats induced by N $\omega$ -nitro-L-arginine methyl ester (L-NAME)<sup>8</sup>. The water extract of *Adansonia digitata* L. at a dose of 100 and 200 mg/kg was effective in reducing systolic blood pressure, diastolic blood pressure and average blood pressure. This is because *Adansonia digitata* L. has antioxidant properties by increasing the availability of NO and preventing cell damage due to oxidative stress.

***Vitex pubescens***



Figure 3. *Vitex pubescens*<sup>34</sup>

*Vitex pubescens* (Verbenaceae) is locally called Halban in Peninsular Malaysia. This plant has been used traditionally to treat hypertension and gastrointestinal disorders<sup>35</sup>. Spathulenol is the main compound of *Vitex pubescens* which acts as a smooth muscle vasorelaxant, anti-inflammatory and antioxidant<sup>36</sup>. The leaves of *Vitex pubescens* were shown to have antihypertensive activity tested on Rats<sup>9</sup>. *Vitex pubescens* was extracted with petroleum ether, chloroform, methanol, and water, wherein petroleum ether extract was considered the strongest extract and was selected for fractionation. The Rats given the oral extract every day of 500 mg/kg/day significantly reduced systolic blood pressure and diastolic blood pressure for 14 days of treatment. This is because *Vitex pubescens* has a vasorelaxant effect.

***Cinnamomum zeylanicum***



Figure 4. *Cinnamomum zeylanicum*<sup>37</sup>

*Cinnamomum*, or also known as cinnamon, is a 10-17 m tall tree that grows in South America, Southeast Asia and Australia<sup>38</sup>. Traditionally used in cooking as a flavoring / coloring agent<sup>39</sup>. Generally, the major chemicals reported in cinnamon include coumarin, cinnamic acid, eugenol, and cinnamaldehyde which contribute to its pharmacological properties (as anti-inflammatory, anti-oxidant, anti-diabetes, and anti-obesity)<sup>38</sup>. *Cinnamomum zeylanicum* capsules (containing 500 mg of dry cinnamon powder) have been shown to have antihypertensive activity<sup>10</sup>. Capsules containing 500 mg of cinnamon powder given 3 times a day for 90 days showed a decrease in blood pressure in stage I hypertensive patients. *Cinnamomum zeylanicum* can increase HDL-c, reduce LDL-c and total cholesterol levels temporarily and reduce the average systolic blood pressure of hospitalized patients with moderate clinical course.

### *Catharanthus roseus*



Figure 5. *Catharanthus roseus*<sup>40</sup>

*Catharanthus roseus* is a native plant of Madagascar belonging to the Apocynaceae family. In traditional medicine, the leaves and roots of this plant are widely used in the treatment of diseases<sup>11</sup>. Certain active compounds such as alkaloids contained in *Catharanthus roseus* have hypotensive activity. The intravenous administration of *Catharanthus roseus* at a dose of 1, 3, and 10mg/kg, was able to reduce the mean arterial blood pressure of Rats respectively;  $14.70 \pm 1.21$ ,  $22.00 \pm 2.24$  and  $36.21 \pm 2.65\%$ .

### *Crotalaria burhia*



Figure 6. *Crotalaria burhia*<sup>41</sup>

*Crotalaria burhia* Buch.-Ham, belonging to the family Fabaceae, is commonly found in arid parts of Pakistan, Afghanistan and India<sup>41</sup>. This herb contains glycosides, alkaloids, flavonoids such as quercetin, saponins, and steroids such as  $\beta$ -sitosterol<sup>42</sup>. All parts of this plant are reported to be used in the treatment of hypertension<sup>43</sup>. The aqueous extract of *Crotalaria burhia* leaves showed a very significant reduction in blood pressure at doses of 200 to 1000 mg/kg<sup>12</sup>. *Crotalaria burhia* extract is able to stabilize blood sugar, greatly reduce insulinemia, systolic blood pressure, diastolic blood pressure and fructose-induced heart rate in rabbits.

### *Leersia hexandra*



Figure 7. *Leersia hexandra*<sup>44</sup>

*Leersia hexandra* belongs to the Poaceae family which is used in traditional medicine to treat many diseases including hypertension. *Leersia hexandra* is widely grown in tropical and subtropical countries and hot regions of Africa. *Leersia hexandra* (Poaceae) water extract was shown to have antihypertensive activity tested on ethanol-induced Wistar Rats<sup>13</sup>. Water extract given intraperitoneally at a dose of 100 and 200 mg/kg was able to reduce the mean arterial pressure (MAP) because *Leersia*

*hexandra* has an antioxidant effect that protects tissue and cell damage due to free radicals from ethanol metabolism.

### *Moringa oleifera* L.



Figure 8. *Moringa oleifera* L.<sup>45</sup>

*Moringa oleifera* L. or also known as moringa is included in the Moringaceae family. This plant is generally used as food and medicine. Methanol and ethyl acetate extracts of *Moringa oleifera* L. have been proven to have antihypertensive activity tested on Rats induced by N $\omega$ -nitro-L-arginine methyl ester (L-NAME)<sup>14</sup>. The extract given at doses of 100 and 300 mg/kg, respectively, showed a hypotensive effect. *Moringa oleifera* L. significantly reduced systolic blood pressure ( $90.97 \pm 0.7975$  mm Hg) in Rats treated with methanol extract and ( $87.71 \pm 0.9623$  mm Hg) in Rats treated with ethyl acetate extract.

### *Allanblackia floribunda*



Figure 9. *Allanblackia floribunda*<sup>46</sup>

*Allanblackia floribunda* Oliver (Clusiaceae) is a medicinal plant widely used in Africa to treat hypertension and many other ailments. The water extract of *Allanblackia floribunda* was shown to have antihypertensive activity tested on ethanol-induced male Wistar Rats<sup>15</sup>. The extract at a dose of 200 and 400 mg/kg significantly reduced blood pressure by an average of 14.06% and 23.25% at each dose. This is because *Allanblackia floribunda* is an antioxidant that can suppress the inflammatory process caused by alcohol.

### *Holarrhena floribunda*



Figure 10. *Holarrhena floribunda*<sup>47</sup>

*Holarrhena floribunda* (G. Don) T. Durand & Schinz is a tree that can grow up to 25 m with its organs in the form of white sap. Generally, this plant grows in African countries and is traditionally used for the treatment of dysentery, diarrhea, fever, snake bites, infertility, venereal disease, diabetes, hypertension, and malaria. Water-ethanol extract of *Holarrhena floribunda* has

shown to have antihypertensive activity tested in rabbits<sup>16</sup>. The extract was administered intravenously at a dose of 10, 20, 40, 80 mg/kg and was able to reduce systolic blood pressure, diastolic blood pressure and mean arterial pressure. The hydro-ethanol extract of *Holarrhena floribunda* stem bark has antihypertensive and antioxidant properties, of which a dose of 40 mg/kg is considered the most effective.

#### *Berberis vulgaris*



Figure 11. *Berberis vulgaris*<sup>48</sup>

*Berberis vulgaris* is a plant that is widely used in traditional medicine<sup>17</sup>. Aqueous extract of *Berberis vulgaris* root bark was proven to have antihypertensive activity tested on Rats. The water extract of *Berberis vulgaris* root bark given intravenously at different doses of 1, 10, and 20 mg/kg showed a hypotensive effect, where at doses of 10 and 20 mg/kg had the most effect on lowering mean arterial blood pressure for more than one hour and returned to baseline there after 106±12.36 minutes and 193±13.94 minutes respectively. The active alkaloid content of the root bark of *Berberis vulgaris* is very effective as an antihypertensive by inhibiting peripheral vascular resistance.

#### *Morinda citrifolia* L.



Figure 12. *Morinda citrifolia* L.<sup>49</sup>

*Morinda citrifolia* L. is a plant that contains antioxidants and is widely used to treat dyslipidemia, inhibits the activity of angiotensin con-verting enzyme (ACE), as an analgesic, and is used for the treatment of hypoglycemia<sup>50</sup>. The ethanol extract of *Morinda citrifolia* L. leaves and fruit was shown to have antihypertensive activity against dexamethasone-induced male Wistar Rats<sup>18</sup>. Leaves ethanol extract (MCLEE) and fruit ethanol extract (MCFEE) can each show a hypotensive effect because they contain flavonoids and antioxidants that can prevent cell damage due to oxidative stress, where the combination of leaves ethanol extract (MCLEE) 500 mg/kg BW and fruit ethanol extract (MCFEE) of 500 mg/kg BW showed the highest hypotensive activity with a combination of MCLEE and MCFEE 1: 1 reducing systolic blood pressure by 16.71 + 3.95%, diastolic blood pressure by 21.49 + 7.90%, and pressure arterial blood on average by 19.58% + 6.35.

#### *Ficus carica*



Figure 13. *Ficus carica*<sup>51</sup>

*Ficus carica* Linn. (Moraceae) has been widely used for the treatment of cardiovascular diseases. The water-methanol extract of *Ficus carica* fruit was shown to be able to show antihypertensive effects tested on glucose-induced Rats<sup>19</sup>. The water-methanol extract given at doses of 250, 500, and 1000 mg/kg, respectively, showed a decrease in blood pressure, where the dose of 1000 mg/kg showed the most effective antihypertensive effect. *Ficus carica* is a plant that is rich in polyphenols, thus it has an antioxidant effect that can prevent cell damage due to oxidative stress.

#### *Bidens Pilosa*



Figure 14. *Bidens pilosa*<sup>52</sup>

*Bidens pilosa* is a medicinal plant belonging to the Asteraceae family which is found mostly in tropical and hot regions of Africa, including Cameroon. This herb is used in traditional medicine for at least 40 disease categories, including hypertension<sup>53</sup>. The ethylene acetate extract of *Bidens pilosa* was proven to have antihypertensive activity which was tested on Rats induced by N $\omega$ -nitro-L-arginine methyl ester (L-NAME). The ethylene acetate extract of *Bidens pilosa* at a dose of 75 and 150 mg/kg in vivo can lower blood pressure without affecting heart rate<sup>20</sup>.

#### *Panax ginseng*



Figure 15. *Panax ginseng*<sup>54</sup>

Korean red ginseng (*Panax ginseng*) is ginseng originating from Korea which contains saponins, ginsenoside Rg3 which can provide a protective effect against hypertension<sup>55</sup>. The ethanolic extract of Korean Red Ginseng Root was shown to have antihypertensive activity by testing Wistar male rats<sup>21</sup>. The ginsenoside content in this plant can have the effect of decreasing renin activity and inhibiting ACE. Giving ethanol extract orally at a dose of 500 and 1000 mg/kg BW for 8 weeks each can reduce

blood pressure, where at a dose of 1000 mg / kg BW gives the most effective results because it can increase NO levels by 52%.

#### *Lantana camara*



Figure 16. *Lantana camara*<sup>56</sup>

*Lantana camara* belongs to the Verbenaceae family and is widely used in the treatment of various diseases. The ethanol extract of *Lantana camara* was shown to be able to show antihypertensive effects tested on NaCl-induced wistar albino Rats<sup>22</sup>. Ethanol extract at doses of 200 and 400 mg/kg showed that it could lower the mean arterial blood pressure by balancing ionic levels, reducing sodium and increasing potassium levels in salt-induced hypertensive Rats.

#### *Allium sativum*



Figure 17. *Allium sativum*<sup>57</sup>

*Allium sativum*, or otherwise known as Garlic, is commonly used throughout the world for both culinary and medicinal purposes<sup>58</sup>. Gamma-glutamylcysteines are compounds present in garlic that can lower blood pressure by inhibiting the conversion of Angiotensin I to Angiotensin II. Garlic at doses of 300 mg, 600 mg, 900 mg, 1200 mg and 1500 mg in divided doses per day for 24 weeks each showed a significant reduction in systolic and diastolic blood pressure in stage I hypertensive outpatients<sup>23</sup>.

#### *Apium graveolens*



Figure 18. *Apium graveolens*<sup>59</sup>

*Apium graveolens*, or commonly known as celery, is a species of plant from the Apiaceae family. Celery grows to a height of 1 m and has odd-pinnate compound leaves<sup>60</sup>. In recent pharmacological studies, celery has demonstrated antioxidant, hypolipidemic and anti-inflammatory activity. Therefore, it can be used as an antihypertensive agent in traditional medicine. *Apium graveolens* celery seed extract has been shown to have antihypertensive activity tested on Rats induced by deoxycortisone acetate<sup>24</sup>. The hexane, methanol, and water-

ethanol extracts administered intraperitoneally were able to lower blood pressure respectively, whereas 300 mg/kg hexane extract was significantly more effective in lowering blood pressure than the other extract groups (methanol and water-ethanol groups).

#### *Vitex cienkowskii*



Figure 19. *Vitex cienkowskii*<sup>61</sup>

*Vitex cienkowskii* (Verbenaceae) is commonly used in traditional Cameroonian medicine to treat cardiovascular disease. *Vitex cienkowskii* contains flavonoids, cyclic penta-triterpenoids (oleanolic acid, maslinic acid, and ceramide). Methanolextract of *Vitex cienkowskii* (Verbenaceae) was shown to have antihypertensive activity tested on male Wistar Rats induced by N $\omega$ -nitro-L-arginine methyl ester (L-NAME)<sup>25</sup>. The methanolic extract administered intravenously at a dose of 40 mg/kg caused mean arterial pressure in the rats. Extracts of *Vitex cienkowskii* have antioxidant activity which can provide protection to blood vessels by increasing NO levels.

#### *Achillea wilhelmsii*



Figure 20. *Achillea wilhelmsii*<sup>62</sup>

*Achillea wilhelmsii* is the main species grown in Iran which is used in traditional medicine. This plant contains alkaloid chemical compounds (Achilleine), cineol, borneol,  $\alpha$  and  $\beta$  pinen, luteolin, apigenin, lignans, camphor, caryophyllene, rutin and carvacrol<sup>63</sup>. The ethanol aqueous extract of *Achillea wilhelmsii* was shown to have antihypertensive activity in rabbits<sup>26</sup>. Ethanol extract intravenously at a dose of 20, 40, and 80 mg/kg, respectively showed a hypotensive effect where at a dose of 80 mg/kg the most effective at reducing blood pressure significantly ( $16.7 \pm 1.4$  mmHg) and does not have a significant effect on heart rate. This is because the aqueous-ethanolic extract has a vasorelaxant effect.

## CONCLUSION

Based on the aforementioned description, it can be concluded that each plant has different secondary metabolites, and each plant used different activity testing methods and administration doses, thus each plant showed different antihypertensive activities.

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