

Literature Review: The Effectiveness of Apigenin Phytochemicals in Lowering Blood Pressure

Studi Literatur: Efektivitas Fitokimia Apigenin dalam Penurunan Tekanan Darah

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ABSTRACT

Background: High blood pressure or hypertension is a non-communicable disease, but it is one of the leading causes of death in the world. In 2023, the World Health Organization (WHO) stated that 46% adults suffer from hypertension and most are unaware of it. One of the treatments for hypertension is to use non-pharmacological, namely apigenin-type flavonoids. Apigenin has antioxidant, anti-inflammatory, and anti-apoptosis activity so it has the potential to lower blood pressure with a decrease in oxidative stress.

Objective: This study aims to examine the effectiveness of apigenin on blood pressure reduction based on existing literature.

Methods: Secondary data were obtained from searching scientific articles through the PubMed and Science Direct databases within the last five years (2020-2024). After screening, four scientific articles met the criteria and could be used to continue this research.

Result: The results of the literature review reported that apigenin is a type of flavonoids that lower blood pressure by preventing blood vessels from narrowing by reducing oxidative stress and inflammation. Apigenin is known to have a Pthalide element that can relax blood vessels, allowing blood output from the heart to be smooth and slowly blood pressure will return to normal. Apigenin is also known to help prevent kidney damage caused by low-fat diets. Studies also show that apigenin can increase nitrate oxidation, reduce oxidative stress, and reduce the risk of atherosclerosis.

Conclusion: This review concluded that apigenin can be a non-pharmacological drug in lowering blood pressure by decreasing oxidative stress. In addition, apigenin can be antioxidant, anti-cancer, anti-inflammatory, and anti-bacterial. However, the right dose to lower blood pressure still needs further research.

Keywords: Apigenin, Hypertension, Oxidative stress

ABSTRAK

Latar Belakang: Tekanan darah tinggi atau hipertensi termasuk penyakit tidak menular, namun penyakit tersebut merupakan salah satu penyebab utama kematian di dunia. World Health Organization (WHO) tahun 2023 menyatakan bahwa orang dewasa yang menderita hipertensi sebesar 46% dan sebagian besar tidak menyadarinya. Salah satu penanganan hipertensi adalah dengan menggunakan non-farmakologi yakni flavonoid jenis apigenin. Apigenin memiliki aktivitas antioksidan, anti-inflamasi, dan anti-apoptosis sehingga memiliki potensi untuk menurunkan tekanan darah dengan penurunan stres oksidatif.

Tujuan: Penelitian ini bertujuan untuk mengkaji bagaimana efektivitas apigenin terhadap penurunan tekanan darah berdasarkan literatur yang ada.

Metode: Data sekunder didapatkan dari pencarian artikel ilmiah melalui database PubMed dan Science Direct dalam kurun waktu 5 tahun terakhir (2020-2024). Setelah dilakukan skrining, terdapat 4 artikel ilmiah yang memenuhi kriteria dan dapat digunakan untuk melanjutkan penelitian ini.

Hasil: Hasil kajian literatur melaporkan bahwa apigenin merupakan salah satu jenis flavonoids yang menurunkan tekanan darah dengan mencegah pembuluh darah menyempit dengan cara penurunan stres oksidatif dan inflamasi. Pada apigenin, diketahui memiliki bagian Pthalide yang dapat merilekskan pembuluh darah, sehingga memungkinkan keluaran darah dari jantung menjadi lancar dan secara perlahan tekanan darah akan kembali normal. Apigenin juga diketahui dapat membantu mencegah kerusakan ginjal akibat diet rendah lemak. Studi juga menunjukkan bahwa apigenin dapat meningkatkan oksidasi nitrat, mengurangi stres oksidatif, dan mengurangi risiko aterosklerosis.

Kesimpulan: Kajian ini dapat disimpulkan bahwa apigenin dapat menjadi obat non-farmakologi dalam menurunkan tekanan darah dengan cara penurunan stres oksidatif. Selain itu, apigenin dapat menjadi antioksidan, anti-kanker, anti-inflamasi, dan anti-bakteri. Namun, dosis yang tepat untuk menurunkan tekanan darah masih membutuhkan penelitian lebih lanjut.

Kata Kunci: Apigenin, Hipertensi, Stres oksidatif

INTRODUCTION

Blood pressure that exceeds 140 mmHg in systolic and 90 mmHg in diastolic is called hypertension. Hypertension is a risk factor for cardiovascular disease and the leading cause of global mortality. This disease can occur without symptoms, so it is often associated with the term “the silent killer”. The WHO states that 46% of adults suffer from hypertension, but do not realize it. Based on data from the *Survei Kesehatan Indonesia* (SKI) in 2023, the prevalence of hypertension in terms of measurement results in the population aged ≥ 18 years was 30.8%. When viewed by age group, the highest prevalence is the age group 65-74 years at 57.8% and age 75 and over at 64% (Kementerian Kesehatan Indonesia, 2023). One of the global targets for infectious diseases is to reduce the prevalence of hypertension by 33% between 2010 and 2030 (World Health Organization, 2023).

People's limited knowledge about hypertension and information about drugs is a barrier to success in the healing process. In preventing high blood pressure, two methods can be used, namely pharmacology and non-pharmacology (Lazdia *et al.*, 2020). Pharmacologic therapy is feared to have long-term side effects such as cardiac arrhythmias, allergies, fluid retention, fatigue, headache, and cough. Experimental studies have supported the potential effects of apigenin, quercetin, and silibinin as beneficial supplements in cohorts at cardiovascular risk (Tomou *et al.*, 2023). The scientific evidence proves that in choosing hypertension drugs, tolerability cannot be used if it only lowers blood pressure (Simamora *et al.*, 2021). This treatment is carried out by taking antihypertensive drugs. Meanwhile, non-pharmacological therapy generally uses herbs, such

as bay leaf decoction and carrot juice (Nuraisyah & Saputri, 2023; Rochmah *et al.*, 2024). Setting a healthy lifestyle, such as not smoking, not consuming alcohol, maintaining an ideal body weight, exercising, and reducing salt consumption, can also help lower blood pressure (Nuraisyah & Saputri, 2023).

Flavonoids are a type of polyphenol that is abundant in fruits and research evidence increasingly shows the antihypertensive effect of flavonoids due to their antioxidant properties. One of the treatments for hypertension is to utilize flavonoids of the apigenin type. Apigenin is a type of flavonoid that has antioxidant, anti-inflammatory, and anti-apoptotic activities (Xu *et al.*, 2022). These effects have been reported to be beneficial in the treatment of atherosclerosis, stroke, hypertension, ischemia or reperfusion-induced myocardial injury, diabetic cardiomyopathy, and provide protection against drug-induced cardiotoxicity (Thomas *et al.*, 2023). When used in combination with other drugs, apigenin increases the efficacy of those drugs, reduces the risk of side effects, and improves response to chemotherapy (Allemailem *et al.*, 2024). Apigenin contains lower toxicity than other flavonoids and is the most well-known compound because it has many organoleptic and nutritional characteristics (Putri & Astuti, 2023). Apigenin in celery acts as a beta blocker, which can lower the heart rate and strength of heart contractions. As a result, less blood flow is pumped and blood pressure is lower (Simamora *et al.*, 2021). The purpose of this study is to find out how effective apigenin is in lowering blood pressure.

METHODS

In this study, the literature review method was used. Literature review is a reproducible, systematic, and explicit method of identifying, assessing, and synthesizing the results of previous research and thinking conducted by researchers and practitioners (Ulhaq & Rahmayanti, 2020). Secondary data were obtained from the publication of scientific articles in journals online through the PubMed and ScienceDirect sites in the last five years, namely 2020-2024. In the journal search,

several keywords relevant to the research topic were used using English), namely "Effectiveness Apigenin for Reducing Blood Pressure." Scientific articles with literature review design, systematic review, and meta-analysis were excluded in this study. After that, journals that met the criteria will be further analyzed for data presentation and conclusions drawn. In this study, based on search and selection by one author, there are four articles that fulfilled the criteria and could be used to continue this research.

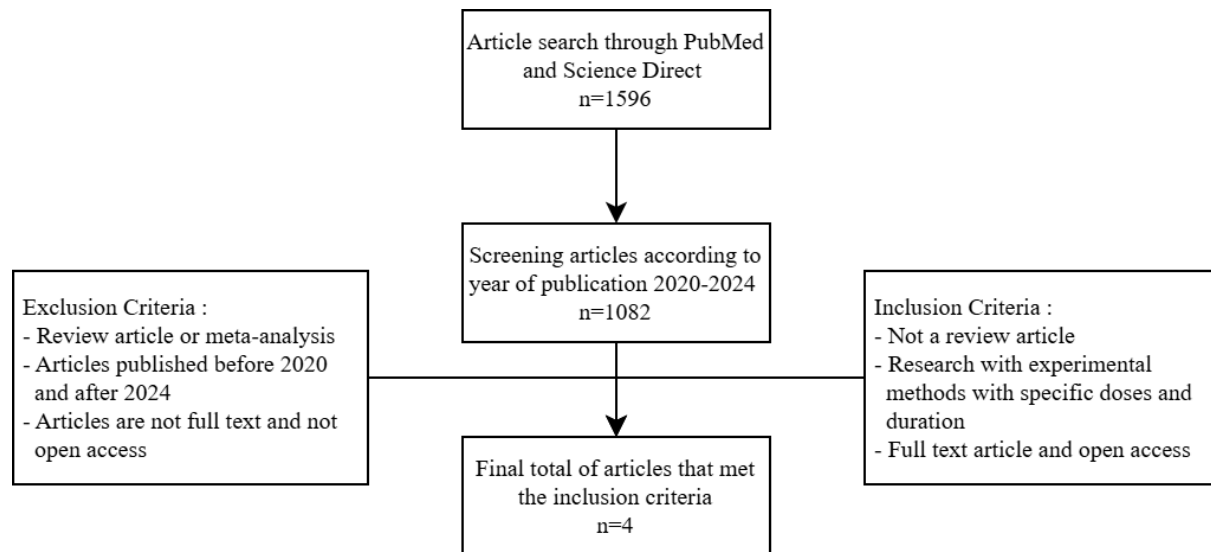


Figure 1. Research Article Selection Procedure

RESULTS AND DISCUSSION

After conducting an article search on the effectiveness or role of apigenin in lowering blood pressure by applying inclusion criteria, the researcher conducted a further review and selected articles that could meet the criteria to meet the requirements in the advanced analysis process. There are 1596 articles from search results from

PubMed and ScienceDirect sources. After that, the articles were re-selected based on the parameters needed in the study so that as many as four suitable articles were obtained and could be used for research materials in analyzing the effectiveness of apigenin in lowering blood pressure. The results of the literature search are described in Table 1 as follows:

Table 1. Literature Search Result

Research Design	Method	Dose	Duration	Result	Reference
In vivo with C57BL/6 mouse subjects and TRPV4 knockout mice (TRPV4 KO)	Subjects were divided into three groups, namely: Normal Diet (ND), High-Fat-Diet (HFD)–60% calories from fat, and High-Fat Diet with added apigenin (HFD+Apigenin)–60% calories from fat with 0.2% apigenin in the diet. Blood pressure was measured periodically during the experimental period by the tail-cuff method. Data were collected and analyzed using one-way ANOVA and t-test to compare differences between groups.	The dose of apigenin used was 0.2% of the total diet given to rats. The maximum tolerated dose is estimated to be around 240 mg/kg.	Duration of treatment for 16 weeks.	Apigenin was able to reduce systolic and diastolic blood pressure in rats with hypertension resulting from a high-fat diet. The decrease in blood pressure was also found to be close to the normal diet group. Therefore, apigenin has potential as a non-pharmacological intervention for obesity-related hypertension, either through enhancement adiponectin and reduction of adipose inflammation.	(Mou <i>et al.</i> , 2024)
In vitro antioxidant activity CE. Cr measured with DPPH Assay	Some of the steps and techniques carried out are starting with collecting plant material identified by a botanist, extra coarse preparation of Caralluma edulis, followed by the induction of hyperlipidemia by providing a high-fat diet and different dosage treatments, then biochemical, histological analysis, antioxidant activity, active components, and statistical analysis to see the significance of the results.	This study tested the effects of Caralluma edulis in hypertension, Dosage given that is: 1. Dose Intravena: 1, 3, 10, dan 30 mg/kg of Caralluma edulis extract. 2. Diuretic dosage: 100, 300, and 500 mg/kg of Caralluma edulis extract.	The duration of the experiment was 28 days so that the researcher had time to evaluate Caralluma edulis against hyper-lipidemia, hypertension, and atherosclerosis in experimental animals.	Caralluma edulis shows anti-obesity potential, has significant hypotension (anti-hypertension) effects, decreases the levels of total cholesterol, triglycerides, and LDL, has antioxidants in fighting oxidative stress, and the presence of bioactive compounds such as apigenin, chlorogenic acid, caffeic acid, and naringenin.	(Akram <i>et al.</i> , 2023)
The study was conducted in vivo by means of treated standard and	Experimental method on rats fed a high-fat diet. Urine, serum, and plasma samples were collected	The dose of apigenin used is 50 mg/kg/day.	The duration of the trial was 12 weeks and all treatments were given daily. Every	The study found that the apigenin has an effect as antioxidant and anti-inflammatory so	(Aldayel, 2022)

Research Design	Method	Dose	Duration	Result	Reference
orally treated LFD (HFD and CMC)	which would later be analyzed with ANOVA. At the end of the study, mouse organs such as liver, kidneys, and fat were collected for further analysis, including gene and protein expression analysis to look at the mechanisms by which apigenin works.		change found in food intake, BB, and other parameters was recorded.	that it can relieve kidney damage in mice that received a high-fat diet. Apigenin has also been shown to be able to reduce oxidative stress so that it has an effect on a decrease in blood pressure.	
In vivo through exangu-Squirt heart. Afterwards, vascular endothelial function was measured through ex vivo carotid artery EDD and Endothelium Independent Dilation (EID).	The methods used included the use of mice as test subjects, administration of apigenin through drinking water, oxidative measurement, and formation of foam cells. In addition, aortic stiffness measurements were also carried out using wire myography and arterial blood pressure measurements using the CODA system noninvasive tail-cuff.	The dose of apigenin used in this study was 0.5 mg/mL in drinking water, which is equivalent to 50 mg/kg/day in rats. This application is effective and does not affect water consumption in any rat age group.	Trial duration of 6 weeks includes measurements of nitric oxide availability, oxidative stress, as well as formation of foam cells in apigenin-treated mice.	Apigenin is able to restore endothelial function, reduce aortic stiffness, and reduce inflammation blood vessels in the process aging. Apigenin is also known to be able to increase the availability of nitric oxide, reduces oxidative stress, and prevents the formation of foam cells that are the initial stage of atherosclerosis. This shows that apigenin has an influence on blood pressure and cardiovascular disease risk.	(Clayton <i>et al.</i> , 2021)

Apigenin

Apigenin is a flavonoid compound found in some fruits and vegetables, and it is known for its health benefits, such as antioxidant and anti-inflammatory properties. Apigenin also shows potential in improving sleep quality and prolonging life, as well as reducing tumor polyference (Kramer & Johnson, 2024; Siddiquee *et al.*, 2025). Apigenin can be found in fruits (oranges, dragon fruit),

vegetables (parsley, celery, and onions), spices (chamomile, thyme, oregano, and basil), some beverages (tea, beer, and wine), nuts, and honey Charrière *et al.*, 2024; (Mushtaq *et al.*, 2023; Rahmadayanti *et al.*, 2024). Apigenin is a bioflavonoid that is known to reduce anxiety, affect immune health, and modulate hormones. In foods and herbs, apigenin is generally in a more stable

derivative form of apigenin-7-O-glucoside (Nault, 2023).

Apigenin is known to function as an antioxidant, anti-inflammatory, anti-amyloidogenic, neuroprotective, chemoprevent, and cognition-binding substance, and has the potential to be used in the treatment and prevention of Alzheimer's disease. In addition, apigenin can also cause sedation and muscle relaxation, but in this case it depends on the dosage (Putri & Astuti, 2023). This is in line with

the three articles that mention the active role of apigenin itself. The potential therapeutic effects on apigenin encourage exploration of the cardioprotective action of apigenin. Apigenin indicates the possible pharmacological mechanism involved in protection against cardiovascular disease. Therefore, apigenin can be used as a dietary supplement in the treatment of cardiovascular disorders (Thomas et al., 2023). The structure of apigenin and derivatives is:

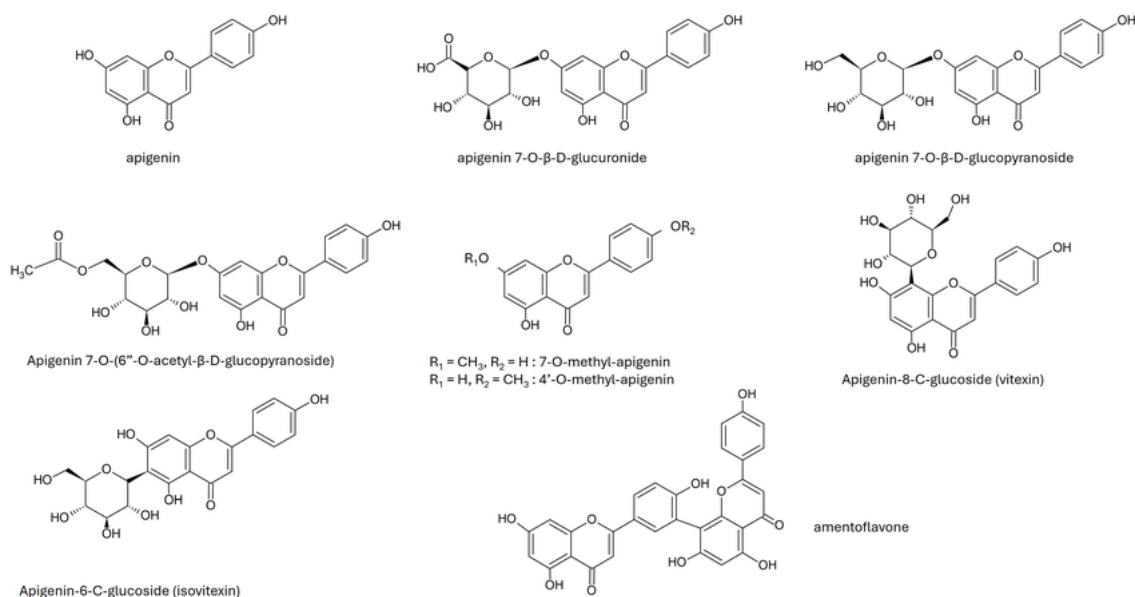


Figure 2. Apigenin and Derivative Structure (Charrière *et al.*, 2024)

Apigenin Intake and Supplementation

A few daily servings of fruits and vegetables can provide adequate amounts of apigenin, which is about less than 5 mg/day for general health needs. Apigenin is considered to have sufficient bioavailability value through these food sources. Some abundant sources of apigenin include chamomile tea (840 mg/100 mg), kumquat (21.87 mg/100 g), artichoke (7.48 mg/100 g), rutabaga (3.85 mg/100 g), sorghum (2.54 mg/100 g), and parsley (215 mg/100 g) (Nault, 2023). Apigenin is shown to have anti-obesity effects by regulating food intake and fat metabolism in the body. However, apigenin dosage recommendations for human intake still require more complex research to determine the optimal dose (Xu *et al.*, 2022). The dosage used in the research of Mou *et al.* (2024) was 0,2% of the total diet given to rats. In the context of rat body weight, the maximum tolerated dose is estimated to be about 240 mg/kg. This research showed that this dosage can have an effect on reducing blood pressure in rats fed a fat diet. Based on calculations using the Meeh-Rubner formula, the recommended dose for humans is estimated to be about 1.6 grams per day for one individual. However, referring to the result of these studies, the recommended dose for human consumption still needs further research to be safe and effective and not cause toxic effects. In

other research, the dose used was divided into two, namely intravenous, gradually starting from 1, 3, 10, and 30 mg/kg of *Caralluma edulis* extract, and the second through diuretics, gradually starting from 100, 300, and 500 mg/kg of *Caralluma edulis* extract. At this dose, researchers can show that with a duration of 28 days, there are significant results in providing a hypotension (anti-hypertensive) effect on the subjects used (Akram *et al.*, 2023). Meanwhile, in research conducted by Aldayel (2022), the dose given was 50 mg/kg per day for 12 weeks. The results showed that apigenin can provide anti-inflammatory and antioxidant effects so that it can relieve kidney damage in mice that received a high-fat diet. Apigenin has also been proven to be able to reduce oxidative stress so that it affects blood pressure reduction. Experiments conducted by Clayton *et al.* (2021) also gave a dose of 0.5 mg/mL in drinking water, which is equivalent to 50 mg/kg/day in mice. This administration was effective and did not affect water consumption in any age group of mice. The duration of treatment in the study was six weeks and the results showed that apigenin was able to restore endothelial function, reduce aortic stiffness, and reduce inflammation of blood vessels in the aging process. Apigenin is also known to increase the availability of nitric oxide, reduce oxidative stress, and prevent the formation of

foam cells which is the early stage of atherosclerosis. This suggests apigenin has an influence on blood pressure and the risk of cardiovascular disease.

Role of Apigenin on Blood Pressure

Apigenin is a type of flavonoid that has been reported to lower blood pressure by preventing blood vessels from narrowing. This effect is greater due to the presence of Pthalide that can relax blood vessels, allowing blood output from the heart to be smooth and gradually blood pressure will return to normal limits (Simamora *et al.*, 2021). One of the vegetables known to contain apigenin and which can lower systolic and diastolic blood pressure in hypertensive patients is celery (Handayani & Widowati, 2020; Nahor *et al.*, 2023; Simamora *et al.*, 2021). Apigenin found in celery leaves acts as a beta blocker that can slow down the heart rate and reduce the strength of the heart's contractions. As a result, less blood flow is pumped and blood pressure is lower (Nahor *et al.*, 2023). Apigenin compounds can provide protection against cardiovascular diseases through anti-inflammatory and antioxidant activities that can protect endothelial cells, regulate cholesterol metabolism, and reduce atherosclerosis plaques formation. Apigenin also has therapeutic potential in the treatment of atherosclerosis, hypertension, and myocardial injury caused by ischemia/reperfusion (Thomas *et al.*, 2023). Mou *et al.* (2024) showed that apigenin had a significant anti-hypertensive effect in obese subjects with hypertension. Specifically, apigenin administration during a high-fat diet was found to reduce the systolic and diastolic blood pressure of these subjects. In fact, the blood pressure of the subjects who received apigenin returned to a level similar to that of the control group that was fed a normal diet. In addition, the experimental results of the *Caralluma edulis* apigenin experiment tested by Akram *et al.* (2023) on mice showed a hypotension effect (anti-hypertension) and contained antioxidants that could reduce oxidative stress so that it is significant in lowering blood pressure. The study mentioned that apigenin may protect the kidneys of mice that receive a high-fat diet by reducing oxidative and inflammation. This can help reduce kidney damage induced by a high-fat diet, including in the context of hypertension. In another study, it was stated that apigenin is able to restore endothelial function, reducing inflammation of blood vessels in the aging process. Case studies have shown that apigenin can increase the availability of nitric oxide, reduce oxidative stress, and prevent the formation of foam cells, which is the first step of atherosclerosis. This suggests that apigenin has the potential to affect blood pressure and the risk of cardiovascular disease associated with aging (Clayton *et al.*, 2021).

Research on the effectiveness of apigenin in lowering blood pressure suggests that this compound

has potential as a natural antihypertensive, which could be an alternative to non-pharmacological therapy with low side effects. However, these studies are often limited to animal models or small samples, so generalization to the human population still requires further validation. In addition, the optimal dose and long-term safety of apigenin have not been fully researched, so it remains a challenge in clinical application.

CONCLUSION

Based on the literature that has been analyzed, it can be concluded that apigenin is one of the most popular types of flavonoids. Apigenin is found in fruits and vegetables. One of the health benefits of apigenin is that it can be a non-pharmacological drug in lowering blood pressure by reducing oxidative stress. In addition, apigenin can be an antioxidant, anti-cancer, anti-inflammatory, and anti-bacterial. However, the right dosage to lower blood pressure still needs further research.

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Conflict of Interest and Funding Disclosure

None.

Author Contributions

NSA: Identify journals, screening journals, analysis, writing, and editing. DRA: writing review and editing.

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