

LITERATURE REVIEW

THE POTENTIAL OF JAMBU KELING (*Syzygium cumini*) LEAVES AS A CANDIDATE FOR HYPERTENSION HERBAL THERAPY: A REVIEW

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Abstrak

Hipertensi atau tekanan darah tinggi adalah kondisi medis serius yang secara signifikan meningkatkan risiko penyakit jantung, otak, ginjal, dan penyakit lainnya. Jumlah orang dewasa dengan hipertensi meningkat dari hari ke hari. Kondisi kesehatan tertentu, seperti diabetes dan obesitas, juga dapat meningkatkan risiko terkena hipertensi. Pengobatan hipertensi adalah perubahan gaya hidup dan obat-obatan. Penderita hipertensi biasanya tidak meminum obatnya karena efek samping dan biaya yang mahal. Terapi herbal sangat berkembang akhir-akhir ini, karena harganya yang murah, ketersediaannya yang melimpah di alam, dan efek samping yang minimal. Penelitian ini bertujuan untuk mengetahui potensi daun *Syzygium cumini* sebagai kandidat terapi herbal hipertensi. Penelitian ini merupakan studi tinjauan pustaka dengan menggunakan data sekunder dari penelitian terkait. Daun *Syzygium cumini* mengandung flavonoid dan/atau triterpen yang memberikan efek antihipertensi melalui kombinasi aktivitas vasodilatasi dan antioksidan dari kelas senyawa ini. Daun *Syzygium cumini* mengurangi tekanan darah dan detak jantung tikus hipertensi spontan dalam beberapa studi in vivo dan in vitro. Efek antihipertensi ini mungkin karena penghambatan tonus arteri oleh blokade masuknya Ca^{2+} ekstraseluler.

Kata kunci: *Syzygium cumini*; Hipertensi; terapi herbal.

Abstract

Hypertension or elevated blood pressure is a serious medical condition that significantly increases the risks of heart, brain, kidney, and other diseases. The number of adults with hypertension increased day by day. Certain health conditions, such as diabetes and having obesity, can also increase the risk for developing hypertension. The treatment of hypertension is lifestyle changes and medication. Patient of hypertension usually do not take their medication due to its side effects and expensive cost. Herbal therapy is very much developed lately, due to its low price, abundant availability in nature, and minimum side effects. The objective of this study is to find out the potential of *Syzygium cumini* leaves as a candidate for hypertension herbal therapy. This research is a literature review study using secondary data from related research. *Syzygium cumini* leaves contains flavonoids and/or triterpenes that exert antihypertensive effects through the combination of the vasodilatory and antioxidant activities of these classes of compounds. *Syzygium cumini* leaves reduces the blood pressure and heart rate of spontaneously hypertensive rats in some of in vivo and in vitro study. This antihypertensive effect is probably due to inhibition of arterial tone by the blockade of extracellular Ca^{2+} influx.

Keywords: *Syzygium cumini*, Hypertension, Herbal therapy.

INTRODUCTION

Hypertension (HTN) is a measurement of systolic blood pressure (SBP) above 130 mmHg and/or a measurement of diastolic blood pressure (DBP) above 80 mmHg. Hypertension is one of the most common chronic diseases characterized by a sustained increase in arterial pressure.^[1] An estimated 1.28 billion adults aged 30-79 years worldwide have hypertension, most (two-thirds) living in low- and middle-income countries.^[2] The results of Riskesdas 2018 show that the prevalence of hypertension in Indonesia based on a national measurement at the age of above 18 years is 34.11%. This prevalence is higher than prevalence in 2013 was 25.8%. There is also an increase of hypertension based on the measurement method also occurs in almost all provinces in Indonesia. The highest prevalence increase was found in DKI Jakarta Province by 13.4%, South Kalimantan by 13.3%, and West Sulawesi by 12.3%.^[3]

Hypertension is the most common preventable risk factor for cardiovascular disease (CVD; including coronary heart disease, heart failure, stroke, myocardial infarction, atrial fibrillation and peripheral artery disease), chronic kidney disease (CKD) and cognitive impairment, and is the leading single contributor to all-cause death and disability worldwide¹⁰. The relationship between BP and the increased risk of CVD is graded and continuous, starting as low as 115/75 mmHg, well within what is considered to be the normotensive range. Successful

prevention and treatment of hypertension are key in reducing disease burden and promoting longevity in the world's population.^[4]

Treatment of hypertension is divided into pharmacological and non-pharmacological treatments.

Non-pharmacological interventions and lifestyle management are recommended for all individuals with hypertension, regardless of age, gender, comorbidity, or cardiovascular risk status. Patient education is paramount to effective treatment and should always include detailed instructions on weight management, salt restriction, smoking control, proper management of obstructive sleep apnea, and exercise. Pharmacological therapy consists of angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), diuretics (usually thiazides), calcium channel blockers (CCBs) and beta-blockers (BBs), which are instituted taking into account age, race and comorbidities such as presence of renal dysfunction, LV dysfunction, heart failure and cerebrovascular disease.^[5,6]

Regardless of the efficiency of the above methods in disease management, they have several disadvantages. These include; undesirable side effects, cost (expensive) and unavailable in many communities. This has led to the use of herbal remedies as an alternative method of treating diseases.^[7]

Herbal therapy is very much developed lately, especially in supportive therapy. This is due to its low price, abundant availability in nature, and minimum side

effects.^[8] One of the promising herbal agents is *Syzygium cumini* leaves extract which contains polyphenols that can act as an antihyperglycemic agents that are good for improving the prognosis and quality of life of Hypertension patients.

RESEARCH METHOD

Method of making this reasearch was literature review using secondary data from previous research. This prototyping study uses a qualitative approach to conceptual analysis, where the research focus is based on pre-existing concepts, which are then understood and developed so that they can be clearly described and put into practice. The aim of this study was to find out the potential of jambu keling (*Syzygium cumini*) leaves extract as a herbal remedy for hypertensive patients to reduce mortality and improve quality of life around the world, especially in Indonesia.

The author uses a literature search engine from national and international indexed journal databases, such as Portal Garuda, Google Scholar, and Pubmed. The inclusion criteria of the literature sources used were in English and Indonesian, from indexed journal publication, were original research, and discussed research according to the keywords, namely hypertension, *Syzygium cumini*, and herbal therapy. The exclusion criteria from secondary data collection are those that do not match the inclusion criteria.

RESULT AND DISCUSSION

Patophysiology of Hypertension

Blood pressure is a number of cardiovascular parameters, such as blood volume and cardiac output (the amount of blood pumped from the heart per minute), and the balance of arterial tone affected by both intravascular volume and neurohumorality. Is determined by. System (discussed in the next section). Maintaining physiological blood pressure levels involves complex interactions of various elements of the integrated nervous system, such as the renin-angiotense sterone system "RAAS", the natriuretic peptide and endothelium, and the sympathetic nervous system "SNS".^[9] The probability of developing hypertension increases with aging, owing to progressive stiffening of the arterial vasculature caused by, among other factors, slowly developing changes in vascular collagen and increases in atherosclerosis.^[10]

The World Health Organization estimates that 47% of ischemic heart disease cases are a direct result of high blood pressure. Even though the epidemiological association between high blood pressure and cardiovascular morbidity and mortality is well known, and despite the fact that sufficient evidence exists to justify antihypertensive treatment, blood pressure is often not adequately controlled. Elevated blood pressure must be due to increased cardiac output, increased peripheral vascular resistance, or both. Each of these mechanisms is in turn regulated by hemodynamic, neural,

humoral and renal processes, the contributions of all of which vary from person to person. With age, the main cause of hypertension is often increased peripheral vascular resistance, often accompanied by increased vascular stiffness, clinical manifestations of isolated systolic hypertension. Familial accumulation implies a genetic predisposition whose interaction with environmental factors (such as salt and calorie intake) and physical activity levels ultimately determines the severity of elevated blood pressure.^[11,12]

***Syzygium cumini* Leaves as Hypertension Herbal Therapy**

Syzygium cumini is known to possess wide range of medicinal properties, which have been attributed to the presence of bioactive compounds in different parts of the plant. The leaves are used in dermatopathies, gastropathies, constipation, leucorrhea, and kidney; fruits are used in the treatment of pharyngitis and splenic diseases; whereas barks are used as astringents, anthelmintic, and carminative.^[13] Polyphenolic and related antioxidant compounds are recognized as important cardiometabolic agents since they scavenge reactive oxygen or nitrogen species and stimulate antioxidant defenses, which may be involved in all the mentioned activities of *Syzygium cumini*.^[14]



Figure 1. *Syzygium cumini* leaves.

Considering *in vitro* studies, methanolic extract of *S. cumini* leaf and branch (1–15 µg/ml) has been shown to strongly act against OH[•] and DPPH[•] radicals, and decreased Fe³⁺ to Fe²⁺ reduction in the FRAP assay. Such activities showed a strong correlation with the high content of polyphenols and flavonoids present in the extract.^[15]

In vivo study stated that antihypertensive and bradycardic effect of *Syzygium cumini* in spontaneously hypertensive rats. The hypotension promoted by hydroalcoholic extract of *Syzygium cumini* leaves was modified by pretreatment with atropine sulfate, as observed in anesthetized rats, suggesting that muscarinic receptors play a role in the hypotensive mechanism of hydroalcoholic extract of *Syzygium cumini*. However, this effect may also be related in part to a reduction in peripheral vascular resistance as a result of the blockade of Ca²⁺ channels.^[16]

The flavonoid contained in *Syzygium cumini* leaves extract have several mechanisms in their function as antioxidants. First,

flavonoid compounds are able to suppress the number of free radicals by donating hydrogen atoms or transferring one electron to free radicals. Second, flavonoids function as chelating agents that allow these compounds to bind to metal ions. Third, the production of free radical-forming enzymes such as xanthine oxidase, protein kinase-C, cyclooxygenase, NADPH oxidase will be suppressed. Fourth, it induces the formation of the body's natural antioxidant enzymes such as superoxide dismutase enzymes, catalase and glutathione reductase.^[17,18]

Syzygium cumini extract reduces the vasoconstrictor activity of calcium in a concentration-dependent manner in endothelial-deprived mesenteric arteries exposed to a depolarizing solution (60 mM KCl, nominally without Ca). This finding suggests that hydroalcoholic extract of *Syzygium cumini* contain components that interfere with vascular smooth muscle responsiveness, possibly acting on the regulation of intracellular calcium levels through voltage-operated calcium channels. Similar results were found in inhibiting the contractile response to calcium in a previous study using a hydroalcoholic extract of *Syzygium cumini* to prepare aortic rings isolated from normotensive rats in the presence of endothelium.^[19]

Natural antioxidants have a variety of biochemical properties, including scavenging of free radicals, inhibition of reactive oxygen species (ROS) production and amendment of cellular redox potential. Inflammation stimulated in response to an infection has been associated with various

diseases such as diabetes, cancer, atherosclerosis and hypertension.^[20] Studies have shown that many plant products, including polyphenols, flavonoids, and various plant extracts, exert antihypertensive effects, possibly due to vasodilatory effects.^[21] Chemical studies on *S. cumini* leaves have shown that chloroform fraction contains phenolic acids, other complex phenolic compounds. Phytochemical screening results indicate that chloroform fraction is enriched in these compounds, which may be related to the vasodilatory properties of the plant.^[22] *in vivo* demonstrate that *S. cumini* L. (Skeels) causes vasorelaxant effect and interfere with the responsiveness of vascular smooth muscle cell, probably as a result of the blockade of Ca²⁺ channel. The *Syzygium cumini* leaves showed an excellent potential as a vasodilator agent for the treatment of hypertension. The findings may provide a possible candidate drug for clinical medical use to treat cardiovascular diseases in the future.^[23]

CONCLUSION

Hypertension is a global health burden with a high economic cost to health systems, and its prevalence is expected to increase significantly in the coming years. It is necessary to carry out intervention strategies that are deliverable at scale to delay the onset/progression, improving prognosis, and patient's life quality of hypertension, one of them by developing *Syzygium cumini* leaves as an antihyperglycemic herbal therapy agent. Before in vitro and in vivo study showed that *Syzygium cumini* leaves extract have a potential for development hypertension

herbal therapy considering antihypertensive of Ca²⁺ channel blocker, antioxidant activity, bioavailability, effectiveness, and minimum side effects.

Furthermore, we suggest to continue this kind of research to clinical studies as a candidate for standardized herbal medicine and as a phytopharmacology. Then, it needs to develop this food ingredients as food products that have protective capabilities in the prevention and treatment of hypertension to obtain

food product certification and arrange the market analysis for future.

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