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Apium graveolens FOR THE TREATMENT OF CARDIOVASCULAR DISEASE: A REVIEW

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ABSTRACT
Cardiovascular disease (CVD) is the world's leading killer, accounting for 30% of deaths. The WHO report states that CVD kills 17.9 million people per year, with an estimated 22.2 million deaths from CVD projected for 2030. Meanwhile, the death rate increases with age. Based on gender, the death rate due to CVD in women (51%) is higher than in men (42%). To reduce and prevent CVD, most people rely on traditional plant-based medicines in addition to or in preference to commercially available medicines to help reverse the disease. One of the best-known medicinal plants for treating CVD is *Apium graveolens*. The active phytochemicals found in this plant are flavonoids, polyphenols, plant sterols, plant sulfur compounds, and terpenoids. The general mechanism of action of flavonoids is to prevent LDL oxidation, which causes vasodilation. Plant sterols prevent CVD by reducing cholesterol absorption in the blood. Plant sulfur compounds also prevent CVD through activation of Nrf2 and inhibition of cholesterol synthesis. Quinones reduce the risk of CVD by increasing ATP production in mitochondria, while terpenoids reduce atherosclerotic lesions in the aortic valve. This review article focuses on the effects of the plant of *A. graveolens* on the treatment of CVD.

KEYWORDS: *Apium graveolens*, Cardiovascular diseases, Phytochemicals.

INTRODUCTION

A condition affecting the coronary blood vessels and the heart, cardiovascular disease (CVD), is identified as such.[1] High blood pressure is the most potent cause and most prevalent risk factor for cardiovascular disease.[2] Additionally, researchers have identified hyperlipidemia, an abnormal lipid metabolism, as a risk factor for cardiovascular disease.[3,4] Cardiovascular disease (CVD) encompasses a wide range of conditions, including peripheral vascular disease, dyslipidemia, hypertension, dyslipidemia, cardiomyopathy, stroke, heart failure, and heart attack.[5,6] Globally, cardiovascular disease is a prominent contributor to both mortality and morbidity. In recent decades, it has emerged as one of the most substantial and swiftly expanding public health concerns.[7] Following acute cardiovascular events (e.g., coronary heart disease, stroke, heart failure, and aortic disease), the mortality rate and prognosis for women are significantly lower in comparison to men. 22.2 million deaths attributed to CVD in 2030, according to the World Health Organization (WHO).[8] Currently, reports indicate side effects and high costs associated with frequently prescribed conventional medications for the treatment of cardiovascular disease.[9,10] Consequently, alternatives that are safer, more cost-effective, and more efficient are required.[11,12] Medicinal plants are the preeminent therapeutic alternative in this context with respect to cardiovascular diseases.[13] The increased understanding of the ways in which herbs enhance health and quality of life has contributed to the widespread acceptance of herbal medicine in the medical field.[14,15]

Ongoing investigations aim to identify novel pharmaceuticals for CVD derived from natural sources. One such approach is the examination of active compounds present in natural ingredients, with a particular focus on medicinal plants that have historically been employed to treat CVD in different nations.[16-18] One such plant is celery (*Apium graveolens*). These active compounds in celery are believed to reduce blood pressure by stimulating urine output (diuretic effect), relaxing blood vessels, preventing blood vessel constriction, and preventing atherosclerosis. Certain individuals in Indonesia are cognizant of the utilization

of *A. graveolens* as a natural remedy for cardiovascular disease.[19] The purpose of this article is thus to present a comprehensive analysis of the efficacy of *A. graveolens* as a therapeutic intervention for CVD.

Taxonomic Classification

Kingdom: Plantae
Phylum : Magnoliophyta
Class : Magnoliopsida
Subclass: Rosidae
Order : Apiales
Family : Apiaceae
Genus : Apium
Species : *Apium graveolens* L.

***Apium graveolens* For The Treatment Of Cardiovascular Disease**

Antihypertensive

Elevated blood pressure is an important risk factor for coronary heart disease, which is the largest cause of death in developed countries.[20] Hypertension (HTN) is called the silent killer, a chronic disorder without symptoms that, if undetected and not treated, will silently damage the blood vessels, heart, brain, and kidneys.[21] Research has shown that adopting a health-promoting lifestyle, losing weight, and reducing NaCl intake can lower the risk of developing HTN. Drug therapy is expected to be necessary if these interventions are inefficient in lowering blood pressure.[22] To achieve ideal blood pressure, most hypertension sufferers require treatment with more than one drug.[23] Appropriate combinations of these drugs at lower doses may have additive effects on blood pressure with a lower incidence of side effects. Taking antihypertensive drugs can cause side effects such as headaches, dizziness, tachycardia, fatigue, and sexual dysfunction.[24] Currently, there are many herbal medicines for treating HTN, one of which is *A. graveolens*. Moghadam et al., reported that *A. graveolens* extract administered intraperitoneally at a dose of 300 mg/kg to deoxycorticosterone acetate-induced hypertensive mice significantly reduced blood pressure.[25] In addition, in a randomized, triple-blind, placebo-controlled, and cross-over clinical trial, administration of *A. graveolens* seed extract (1.34 g/day) to patients for 4 weeks was reported to reduce blood pressure significantly and return blood pressure to normal limits.[26]

Antihyperlipidemic

A predictor of coronary artery disease (CAD) is hyperlipidemia. Globally, this disease is becoming increasingly prevalent in both developed and developing nations.[27] A significant risk factor for the development and progression of atherosclerosis is hyperlipidemia. The main signs of this disorder are high levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and low levels of high-density lipoprotein cholesterol (HDL-C).[28] Hence, the primary objective in the management of hyperlipidemia and arteriosclerosis is to mitigate the elevation in lipid concentrations in the blood, serum, and plasma.[29] At the time of publication, hypolipidemic medications had been associated with several concerning adverse effects. These include, but are not limited to, hyperuricemia, muscle damage, impotence, memory loss, peripheral neuropathy, body aches, gynecomastia, and skin rashes. Bidkar et al., also reported that the concurrent use of this medication with others typically results in an elevated incidence of myopathy and rhabdomyolysis.[30] Prolonged use of the majority of hypolipidemic medications may result in improved outcomes, including liver damage.[31] Consequently, the investigation of novel antihyperlipidemia agents derived from botanical substances is imperative. Herbal plants offer numerous benefits in comparison to conventional medicines, such as reduced side effects, widespread cultural acceptance, and simplified accessibility.[32,33] Iyer and Patil reported that *A. graveolens*, a medicinal plant, is used in the treatment of hyperlipidemia. It was reported that oral administration of 500 mg/kg of *A. graveolens* extract to mice with hyperlipidemia demonstrated a significant reduction in total cholesterol, triglyceride, LDL, and VLDL levels while significantly increasing HDL levels.[34, 35]

Treatment for Chronic Heart Failure

Cardiovascular disease is a combination of a collection of disorders that affect the heart and blood vessels. Among them are hypertension, coronary heart failure, stroke, and heart failure (HF).[36] Approximately 17.3 million deaths were estimated to be due to CVD by the WHO in 2013, and this is expected to increase to 23.3 million by 2030.[37] Chronic heart failure (CHF) is a common health problem in the world and a serious subject in clinical cardiology, and its prevalence is more than 23 million worldwide.[38] Management of CHF is carried out using combination therapy with beta-blockers, digitalis, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, diuretics, aldosterone receptor antagonists, and vasodilators, based on international guidelines.[39] Although there have been many advances in the management of CHF, deaths from this disease continue to increase.[40] Researchers need to evaluate new drugs that have been proven or are possible for managing or preventing CHF. Medicinal plants have a good potential source for introducing new medicines.[41] *A. graveolens* is a medicinal plant that can be used to treat CHF. Administration of *A. graveolens* extract at a dose of 100 mg/kg/day intraperitoneally to isoproterenol-induced CHF model mice can significantly improve heart function by improving left ventricular remodeling and reducing high-sensitivity C-reactive protein (hs-CRP) and N-terminal pro-b-type natriuretic peptide (NT-ProBNP) without side effects on the liver or kidneys.[42]

Diuretic

Drug-induced diuresis is beneficial in many life-threatening disease conditions, such as congestive heart failure, nephritic syndrome, cirrhosis, renal failure, and

hypertension. However, currently, most diuretic drugs, such as high-ceiling loops and thiazides, have several side effects, such as changes in electrolytes and metabolism.[43,44] The search for better drugs with lower side effects that are more effective and economical is a current need.[45,46] Plants are a source of various medicines,[47,48] therefore, research to find compounds that have potential as diuretics from plants must continue to be carried out, one of which is empirically explored medicinal plants that have diuretic effects.[49] One of these plants is *Apium graveolens*. Administration of *A. graveolens* extract at a dose of 200 mg/kg orally to diuretic model mice can significantly increase urine output, increase urinary electrolyte excretion (Na^+, K^+, and Cl^- ions), and have better diuretic activity than the standard drug furosemide.[50]

CONCLUSION

A. graveolens has been scientifically proven to be able to treat CVD, and this plant has different mechanisms of action in treating CVD. However, further research must be carried out to see the effectiveness of *A. graveolens* in managing CVD clinically so that it can be developed as an alternative treatment to replace synthetic drugs, which have now shown detrimental side effects.

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