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Review Article

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PROTECTIVE EFFECTS OF ICARIIN ON CARDIOVASCULAR DISEASES – A REVIEW

Shabrina Zahratun Nisa, Adella Marsyanti, Aulia Nursyifa, Dhea Ananda, Diana Karlina, Dini Hakiki, Fitrah Nur Fitriani, Lutvia Ramadhina, Muhammad Rizki Aditya, Nihal Shahifah, Putri Fitriyah Husnul Khotimah, Rifky Syarif, Ristin Prasmawati, Rizma Septia Wahyuningsih, Tarradiva Rosita Fitri, and Maulana Yusuf Alkandahri*

Faculty of Pharmacy, Universitas Buana Perjuangan Karawang, Karawang, West Java, Indonesia.

***Corresponding Author: Maulana Yusuf Alkandahri**

Faculty of Pharmacy, Universitas Buana Perjuangan Karawang, Karawang, West Java, Indonesia.

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ABSTRACT

When the function of the heart and blood vessels is obstructed, cardiovascular disease is the resulting condition. Researchers have identified *Icariin*, a bioactive flavonoid compound from the genus *Epimedium*, as having a protective effect against a range of cardiovascular diseases. As a prenylated flavonol glycoside, this substance is classified. It is a 3,7-O-diglucoside 8-prenyl derivative of kaempferol. At present, *Icariin* has been the subject of numerous scientific investigations that have established its potential as a treatment for a wide range of cardiovascular ailments, including atherosclerosis, hypertension, stroke, heart attack, arrhythmia, heart failure, and hyperlipidemia. The protective potential of *Icariin* against a variety of cardiovascular diseases will therefore be the subject of this review article.

KEYWORDS: *Icariin*, Atherosclerosis, Hypertension, Stroke, Heart attack, Arrhythmia, Heart failure, Hyperlipidemia.

INTRODUCTION

Due to the potential for severe adverse effects associated with ineffective synthetic drugs, retesting is conducted utilizing herbal remedies purported to possess curative properties for cardiovascular disease.[1] *Icariin*, a bioactive compound derived from herbal plants, is specifically identified in plants belonging to the genus *Epimedium brevicornum* Maxim.[2] *Epimedium*, a plant with cultural significance, has been utilized in China, Korea, and Japan for over a millennium. *Icariin* (ICA) is a class of prenylated flavonoids denoted by the molecular formula $C_{33}H_{40}O_{15}$. It is composed of the following functional groups: rhamnosyl at C-7, glucosis group at C-3, methoxyl group at C-4, prenyl group at C-8, and glucosis group at C-3. The primary agent responsible for the pharmacological effects of the substance is the active substitution group C-8.[3] At present, a comprehensive assessment report concerning the potential of ICA to safeguard the body against diverse cardiovascular diseases is absent. Therefore, this review article is aimed to describe the protective impact of ICA with respect to a range of cardiovascular diseases.

Atherosclerosis

Atherosclerosis is a chronic inflammatory disease of the blood vessels that is characterized by the narrowing and hardening of the lumen due to the accumulation of cholesterol and lipids.[4] A researcher reported that administering ICA at a dose of 40 mg/kg/day significantly reduced the size of atherosclerotic plaque in the aorta of ApoE mice by 5.8%. This study showed that ICA attenuated the development of atherosclerosis in several animal models.[5]

Hypertension

Hypertension, or high blood pressure, is defined as a systolic blood pressure above 140 mmHg and a diastolic blood pressure above 90 mmHg. This disease is one of the most significant causes of death worldwide because increased blood pressure is considered a major risk factor for coronary artery disease and its complications, such as heart failure, stroke, kidney disease, and diabetes.[6] Administration of ICA at a dose of 20 mg/kg to 40 mg/kg was reported to reduce rat blood pressure in the spontaneously hypertensive rats (SHR) model.[7] This blood pressure-lowering effect is caused by ICA being able to reduce serum angiotensin II levels, blood pressure, and heart rate, as well as alleviate aortic fibrosis.[8]

Stroke

Stroke is a serious health condition that occurs when blood flow to the brain is blocked and decreased, causing damage to nerve cells.[9] Intraperitoneal administration of ICA at a dose of 60 mg/kg was reported to reduce brain

damage in mice caused by ischemic stroke.[10] This effect is caused by ICA being able to protect the survival of nerve cells by preventing apoptosis and reducing oxidative and nitrosative stress that occurs during stroke.[11]

Heart attack

A heart attack is a disease that occurs when blood flow to the heart completely stops. The cause is plaque rupture, thrombosis, lumen stenosis, or blockage of the coronary arteries.[12] Administration of ICA at a dose of 60 mg/kg p.o. for 28 days was reported to protect rat heart muscle cells and protect against exposure to oxidative stress through activation of ERK signaling in cells.[13, 14]

Arrhythmia

Arrhythmia is a heterogeneous condition where there is abnormal electrical activity in the heart.[15] Intraperitoneal administration of ICA at a dose of 3 mg/kg was reported to increase the duration of the action potential at 50 and 90% repolarization and reduce the amplitude of the action potential (AP) and the maximum upward movement speed of the action potential in left atrial myocytes (LAM) and left ventricular myocytes (LVM). in a rabbit animal model.[16] Meanwhile, in vitro administration of ICA with concentrations of 5 and 10 µM was reported to weaken the level of dependence of action potential duration (APD) on left ventricular mass (LVM).[16]

Heart failure

Heart failure is a medical condition in which the heart cannot pump enough blood to meet the body's supply of oxygen and nutrients.[17] Heart failure is associated with cardiac hypertrophy and changes in cardiac remodeling (cadiocyte shape and size).[18] Researchers reported that administering ICA at a dose of 10 mg/kg inhibits the loss of systolic and diastolic function in the rat heart, thereby demonstrating its cell membrane protective activity.[19] In addition, ICA can also reduce cardiac remodeling in mice with congestive heart failure.[20]

Hyperlipidemia

Hyperlipidemia is an important risk factor in the initiation and progression of atherosclerosis. The main manifestations of this disorder include increased plasma concentrations of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and low concentrations of high-density lipoprotein cholesterol (HDL-C).[21] Administration of ICA at doses of 20, 40, and 80 mg/kg was reported to reduce total cholesterol, triglyceride, and LDL levels as well as increase HDL and significantly improve liver damage in NAFLD mice.[22]

CONCLUSION

Scientific evidence has established that *Icariin* possesses a protective effect against a range of cardiovascular diseases, such as atherosclerosis, hypertension, stroke, myocardial infarction, arrhythmia, heart failure, and hyperlipidemia. It is worth noting that the specific mechanism of action of this compound varies among the tested diseases. However, additional research is required to determine whether *Icariin* is effective in the treatment of various cardiovascular diseases in order to develop it into a viable alternative treatment option.

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