



EFFECTS OF BREADFRUIT LEAF EXTRACT IN REDUCING THE RISK OF CORONARY HEART DISEASE

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ABSTRACT

Coronary heart disease (CHD) is the number one cause of death globally, caused by accumulation of plaque, a mixture of fat, cholesterol, and calcium deposits in the arteries for years which over time causes narrowing and hardening of the coronary arteries so that oxygen supply in the blood decreases. CHD can be potentially prevented with active substances contained by plants such as breadfruit. Breadfruit leaf (*Artocarpus altilis*) is one of the natural ingredients that contain flavonoids, which can reduce cholesterol, triglycerides and LDL in the blood so the risk of CHD will decrease. Objective to describe the potential anticholesterol effects of breadfruit in coronary heart disease caused by high cholesterol. This paper used literature study involving 16 libraries both national and international books and journal. Conclusions: Breadfruit leaf has the effect of preventing the risk of coronary heart disease by lowering cholesterol, triglyceride and LDL levels in the blood without side effects.

Keywords: breadfruit leaf, flavonoid, coronary heart disease

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INTRODUCTION

Non-Communicable Diseases (NCD) is a disease that not transmitted from person to person. Nevertheless, it is 70% the cause of death in the world. One of the NCD that is still a global problem is coronary heart disease. According to the World Health Organization (WHO) coronary heart disease is ranked first as the cause of death in the world. It is estimated that there are 17.9 million cases per year with 31% of the cases causing death of which one third are under 70 years old (WHO, 2017; The George Institute for Global Health, 2017).

Based on data from the Riset Kesehatan Dasar (Riskesdas) in 2018, the prevalence of patient with coronary heart disease tends to increase from year to year. In fact an estimated 2,784,064 inhabitants or 15 out of 1000 people in Indonesia suffer from heart disease and 37% of them cause death, this figure is twice as high as the death rate from cancer. The province with the highest heart disease in Indonesia is North Kalimantan with 2.2% while the province with the lowest heart disease is Nusa Tenggara Timur with 0.7%. This incident will continue to increase, especially in developing countries due to lifestyle

changes(Kemenkes RI, 2018).

Coronary heart disease (CHD) or what is known as coronary artery disease is a disease caused by accumulation of plaque, a mixture of fat, cholesterol, and calcium deposits in the arteries for years which over time causes narrowing and hardening of the coronary arteries so that oxygen supply in the blood decreases. More than 300 risk factors for CHD, but one factor that significantly increases the risk of CHD is high cholesterol. As a risk factor, cholesterol, especially the atherogenic lipoprotein, namely Low Density Lipoprotein (LDL) will be retained in the endothelium and turned into cytotoxic, proinflammatory, chemotactic and proatherogenic which causes endothelial function to decrease(WHO, 1996;National Heart Lung and Blood Institute, 2009; National Heart Foundation of Australia, 2013; Tri, *et al.*, 2014; Herman, *et al.*, 2015; Astuti, *et al.*, 2019).

CHD is generally asymptomatic (without symptoms), but can also be accompanied by symptoms such as pain or discomfort in the chest. Pain is generally felt behind the left breastbone (sternum) and spreads throughout the chest, shoulders, back, left arm, and jaw. The pain can be like pressed, burned, punched, or squeezed. Other complaints can be in the form of disorders of the digestive tract, palpitations to decreased consciousness(Chronic Disease Management and Control Branch, 2012; Herman, *et al.*, 2015).

The increasing prevalence of coronary heart disease certainly must be immediately intervened. Efforts to overcome the disease such as by making lifestyle modifications and treatment must be made. At present, cholesterol-lowering drugs such as statins, fibrates, bile acid sequestrants, niacin, and ezetimibe are often used for primary prevention of CHD. However, most of these drugs have several side effects ranging from mild ones such as gastrointestinal disorders to severe side effects such as cognitive disorders. Therefore, research is needed to look for new compounds with lower toxicity but have the effect of lowering cholesterol that is equal or better than the drug(Adi, 2014).

Herbal medicines have long been used by Indonesian people, this is because herbal medicines are considered cheaper and have relatively smaller side effects than chemical based drugs. This is one of the factor in the emergence of research into traditional herbal medicines as alternative medicines recognized by WHO. One of the plants that can be used as herbal medicines to reduce cholesterol is the leaf of breadfruit (*Artocarpus altilis*) which is a waste and is usually used by the community as animal feeds.

Breadfruit leaf(*Artocarpus altilis*) are reported to have anti-atherosclerotic, anti-lipid, anti-platelet, and anti-inflammatory. Flavonoid function to inhibit the activity of lipogenic enzymes so can reduce triglyceride levels in the blood and will result in the accumulation of fat in the walls of blood vessels is inhibited so that the risk of coronary heart disease decreases. Based on its potential, research for breadfruit is important to be conducted to determine the anticholesterol effect in preventing coronary heart disease. The purpose of this article is to describe the potential anticholesterol effect of breadfruit (*Artocarpus altilis*) in coronary heart disease caused by high cholesterol level(Astuti, *et al.*, 2019).

METHOD

This study uses the literature review method, in which researchers search, combine and analyze facts based on the manual and the latest research traced through the PubMed database and Google Scholar by conducting a review of the title, content and results that discuss the effect of breadfruit leaf on reducing the risk of heart disease. coronary. The library sources used by researchers involved 16 libraries from 1996 to 2019.

RESULTS

Research conducted by Maharani, et al in 2014 showed that phytochemical screening of breadfruit leaf obtained results showing that breadfruit leaf contain alkaloids, phenolic, flavonoids, tannins, and saponins (table 1)(Maharani, *et al.*, 2014).

Table 1.
Phytochemical Screening Results of Breadfruit Leaf (*Artocarpus altilis*)

Phytochemical Test	Result	Explanation
Alkaloids	Cloudly, light-orange color	+
Phenolic	Brown	+
Flavonoids	Red sediment	+
Tannin	Black with green hue	+
Saponin	foamy	+

(Maharani, *et al.*, 2014)

Information:

(+) = Simplicity reacts positively to the reagents tested

(-) = Simplicity reacts negatively to the reagents tested.

Pramono, et al., (2011) found that in white rats (*Rattus norvegicus*) before and after given breadfruit leaf extract (*Artocarpus altilis*) with different doses shown a significant decrease in triglyceride levels ($p < 0.001$). The greatest decrease in total cholesterol, triglyceride, and LDL levels was found at doses of 4.2 ml (figures 1, 2 and 3) (Pramono *et al.*, 2011).

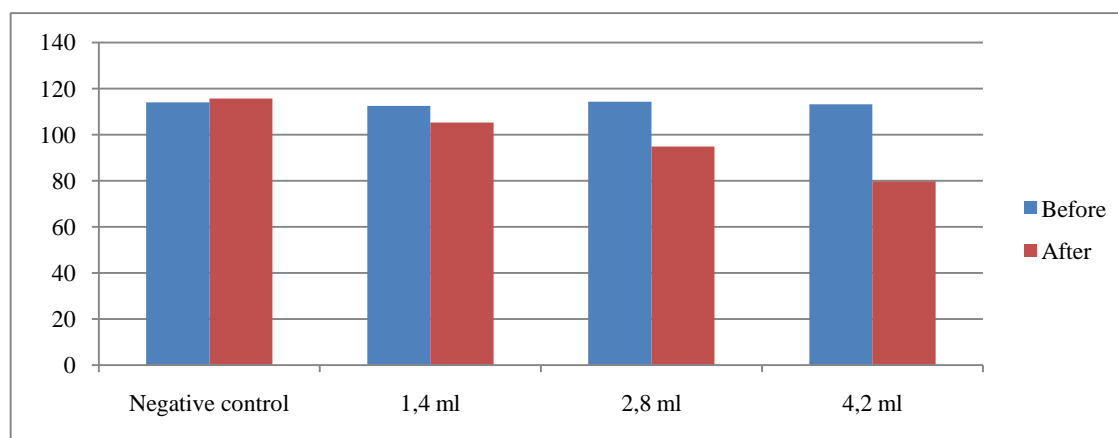


Figure 1.
Average Triglyceride Levels in Various Treatments (Pramono *et al.*, 2011)

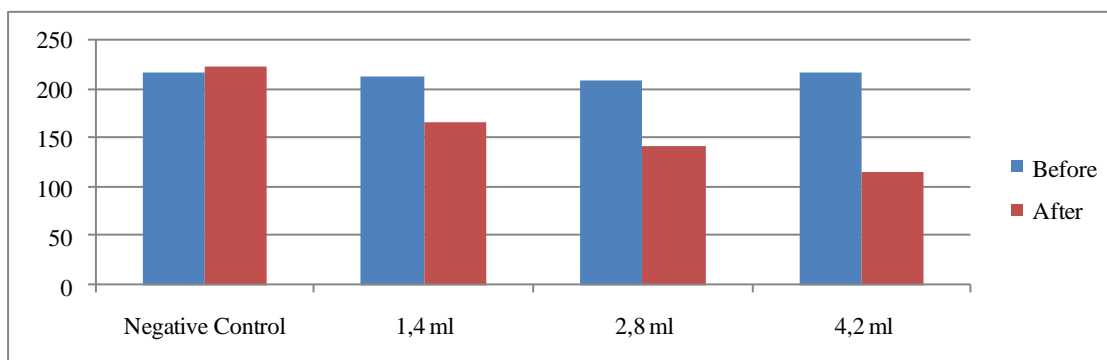


Figure 2.
Average Total Cholesterol Levels in Various Treatments(Pramono *et al.*, 2011)

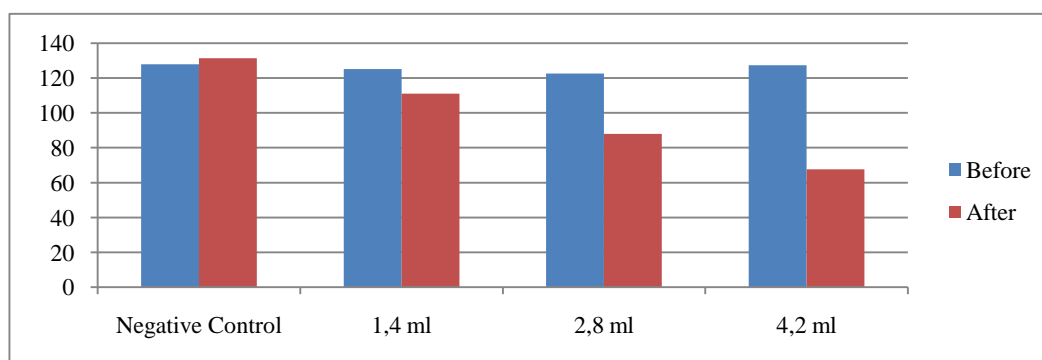


Figure 3.
Average LDL levels in various treatments(Pramono *et al.*, 2011)

Akanni and Oyebimpe (2014) showed in histological examination method of liver with Wistar rats that treatment with breadfruit leaf at a dose of 200 mg/kg reversed the adverse effects of cholesterol on the histological picture of the aorta and rat liver. These histological results corroborate biochemical findings that show the beneficial effects of breadfruit leaf in hypercholesterolemic rats (Figure 4)(Akanni and Oyebimpe, 2014).

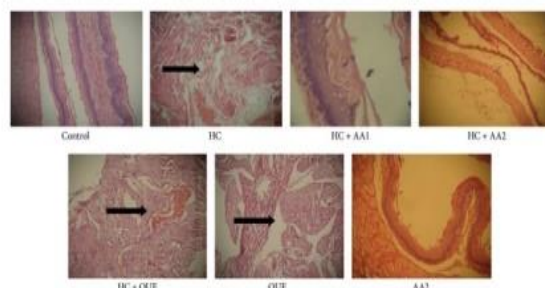


Figure 4.
Histological Examination of Aortic and Liver Hypercholesterolemia Rats (Akanni and Oyebimpe, 2014)

This is similar to the research conducted by Astuti, et al., (2019), using mice (*Mus musculus*), obtained at a dose of 0.0571 ($p = 0.039$) breadfruit leaf decoction has the ability to reduce blood cholesterol levels in mice (Astuti, et al., 2019).

DISCUSSION

Coronary heart disease occurs because of pathogenic process in the arteries and aorta as a consequence of decreased or absent blood flow from stenosis of the blood vessels. CHD involves of multiple factors such as dyslipidemia, immunologic phenomena, inflammation, and endothelial dysfunction. These factors are believed to trigger the formation of fatty streak, which is cause CHD (Jan and Lopez, 2019).

The process of CHD begins with an oxidation process that causes changes in k-LDL to oxidized LDL (Ox LDL). On the other hand, deendothelization occurs with or without the process of platelet adhesion happens over time and cause endothelial dysfunction. Atherogenic LDL (Ox LDL) will be retained and turn into cytotoxic, proinflammatory, chemotactic, and proatherogenic. As a result, endothelial cytokines will be released, whereas NO (Nitrogen monoxide) produced by endothelium decreases so that endothelial dilatation function will be reduced, in addition endothelial will release adhesion cells such as Vascular Cell Adhesion Molecule-1, InterCellular Adhesion Molecule-1, E Selectin, P Selectin and capture monocytes and T cells. Monocytes will turn into macrophages which will capture Ox LDL and turn into foam cells which will then develop into fat nuclei and have a protective fibrous. This fibrous protector is very fragile so that it triggers the process of thrombogenesis which results in the occurrence of acute coronary syndrome (ACS). Impaired function of endothelial dilatation is considered endothelial dysfunction, and apoptotic cells produced by Ox LDL cause plaque and trigger the formation of thrombus This process occurs continuously so that plaque causes narrowing of the coronary arteries that supply oxygen to the heart and its make organs don't get any enough blood, this causes the patient usually feel pain in his chest (Adi, 2014; Baixeras et al., 2014).

Breadfruit (*Artocarpus altilis*) is a food that is often found in Indonesia. Breadfruit is very suitable to grow in tropical climates, especially the hot lowlands, so the distribution of breadfruit in Indonesia is very broad. Some regions in Indonesia have different names for breadfruit. This shows that breadfruit is a fruit that is familiar to people in Indonesia. Breadfruit includes a family of flowering plants (Moraceae) which generally have a height of 17 m to 30 m. Breadfruit can be classified by seeds, namely breadnut (breadfruit seed) and breadfruit (breadfruit without seed). Breadfruit leaf are round with pointed tips and pinnate leaf. The top of the leaf and bones are shiny dark green or yellowish green, while the bottom of the breadfruit leaf is pale green, rough, has fine hair and has a rough texture. Breadfruit leaf have a length of 30-60cm with a width of 20-40cm. Maharani, et al in 2014 showed that breadfruit leaf contain flavonoids which can reduce cholesterol, triglycerides and LDL in the blood so the risk of CHD will decrease (Maharani, et al., 2014; Estalansa, et al., 2018).

Flavonoids are phenol compounds which have a chemical structure of C6-C3-C6, consisting of one aromatic ring A, one aromatic ring B, and a heterocyclic middle ring containing oxygen. Flavonoids function to increase the activity of the lipoprotein lipase enzyme so that triglycerides will be hydrolyzed into fatty acids and glycerol and will circulate in the blood vessels. In addition, flavonoids inhibit the activity of lipogenic enzymes such as DGAT (diacylglycerol acyltransferase) which causes decreased triglyceride levels (Pramono *et al.*, 2011; Tri, *et al.*, 2014).

Based on research that has been done, the flavonoid content in breadfruit is thought an active compound that contributes to the anticholesterol effect. Flavonoids are compounds that are generally found in green plants that have many functions, one of them to reduce triglyceride levels in the blood will result in the accumulation of fat in the walls of blood vessels is inhibited so that the risk of coronary heart disease decreases. In addition, flavonoid compounds contained in breadfruit leaf can reduce LDL levels in the blood. LDL levels are determined by VLDL levels because LDL is formed by VLDL through the lipolytic cascade process. VLDL has a constituent component, namely cholesterol ester and apolipoprotein B, triglycerides, and other lipid components. Flavonoids will cause VLDL levels to decrease by inhibiting transfer proteins namely ACAT (Acyl Co-A Cholesterol Acyl transferase) and MTP (microsomal triglyceride transfer protein) enzymes. The ACAT enzyme plays the role of translating Apo B into the endoplasmic reticulum membrane and catalyzes the cholesterol ester from cholesterol, whereas MTP has a function in the process of triglyceride, cholesterol ester and Apolipoprotein B cholesterol, so that if the ACAT and MTP enzymes are inhibited it will reduce VLDL levels, then LDL and cholesterol levels. the total will decrease (Pramono *et al.*, 2011; Akanni dan Oyebimpe, 2014).

CONCLUSION

Breadfruit leaf has an effect on reducing blood cholesterol, triglyceride and LDL levels significantly. The dose of breadfruit leaf (*Artocarpus altilis*) 200-400mg/kgBW has anti-cholesterol effect and does not cause side effects, so it can be concluded that the breadfruit leaf has the effect of preventing the risk of coronary heart disease by lowering cholesterol, triglyceride and LDL levels in the blood.

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