

REVIEW ARTICLE

Phytochemical Screening and Therapeutic Effects of Binahong (*Anredera cordifolia* (Ten.) Steenis) Leaves

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ABSTRACT

In this review, the function of secondary metabolites in Binahong (*Anredera cordifolia* (Ten.) Steenis) leaves were summarized for their therapeutic effects such as antimicrobial activity, anti-inflammatory, wound healing, lowering the blood pressure, and antihyperlipidemic activity as a potential medicinal plant to treat disease. The phytochemical screening of Binahong leaves extracted by using particular solvent showed positive results to the presence of phenolic, steroid, terpenoid, alkaloid, and saponin compounds contained in the extract. The antimicrobial activity is able to disrupt cell membrane activity and inhibit bacterial growth, meanwhile anti-inflammatory ability is able to decrease anti-inflammatory agents level. It also decreases blood pressure by regulation of lipid metabolites, reduction of peripheral resistance, and upregulation of nitric oxide activity. The ethanolic extract of Binahong leaves can reduce fat deposits or layers in the endothelial cells, cholesterol, triglycerides, and low-density lipoprotein (LDL) cholesterol levels, and decrease the levels of malondialdehyde (MDA formation) from the lipid peroxidation to prevent hyperlipidemia and heart disease.

Keywords: Binahong leaves; *Anredera cordifolia*; phytochemical screening; therapeutic effects

INTRODUCTION

The use of botanical drugs to treat various diseases is often preferred for some people, instead of the use of modern medicine. Botanical drugs use the natural products from nature, such as seed, flower, fruit, and the other parts of the plant that are 'believed' to have some efficacy to be used as drugs for the treatment of the patient. This kind of drug is considered to be safer for the human body, due to the less side effects and toxicity compared to synthetic drugs. The bioactive compounds contained in the botanical drugs are also proven by a lot of

studies and researches to have an intended effect on various diseases (Nisar, Sultan, & Rubab, 2018). For instance, a group of anticancer drugs called vinca alkaloids such as Vinblastine and Vincristine are extracted naturally from Madagascar periwinkle plant or *Catharanthus roseus* which has a cytotoxic effect on cancer cells (Iskandar & Iriawati, 2016). These are the reasons for some pharmaceutical companies to do more research and development in botanical drugs, since their safety, efficacy, and quality are high enough and not inferior to the chemical drugs. In addition to that, the botanical drug also

occupies almost a half of the medicinal supplies on the global market, in which the size of the global market itself is estimated to be approximately 1 trillion dollars with 8 to 10% growth annually. One of the examples of a very successful and profitable botanical drug is Oseltamivir or Tamiflu, which is a botanical drug obtained from *Illicium verum* that had sales of 3 billion dollars from all over the world (Ahn, 2017).

In Indonesia, there are a lot of plants which can be used as botanical drugs, one of them is Binahong. Binahong with the scientific name of *Anredera cordifolia* (Ten.) Steenis is a part of the *Basellaceae* family, and originates from South America.



Figure 1. Binahong (*Anredera cordifolia* (Ten.) Steenis) leaves (Alfisana, 2020).

Binahong leaves are heart-like-shaped with a color of bright and shiny green, have a length of 5 to 10 centimeters and 3 to 7 centimeters wide. Lots of studies have been conducted during the past 6 years to observe the bioactive compounds contained in the Binahong leaves and their potency for being a botanical drug (Abidin *et al.*, 2017; Ariani, Loho, & Durry, 2014). Metabolites that are contained in Binahong leaves such as flavonoid and saponin, have been studied to have therapeutic effects such as antimicrobial activity, anti-inflammatory, wound healing, and

lowering the blood pressure as well as cholesterol level, which can be a great botanical drug to be developed for medicinal purposes. This review will discuss the phytochemical screening of Binahong leaves and its therapeutic effects.

TAXONOMY

Binahong (*Anredera cordifolia* (Ten.) Steenis) is from the genus of *Anredera* Juss. or also called madeira vine. There are two subspecies of *A. cordifolia*, which are *A. cordifolia* subsp. *cordifolia* and *A. cordifolia* subsp. *gracilis*, where these two subspecies are differentiated by some factors such as vegetative morphology, occurrence of fruit with development of seeds, dimension of pollen grain and sculpture of exine, and ploidy level (Julien, McFadyen, & Cullen, 2012). According to the United States Department of Agriculture (USDA) official datasheet (2017), the taxonomic tree of Binahong is:

Kingdom	: Plantae
Subkingdom	: Tracheobionta - Vascular plants
Superdivision	: Spermatophyta - Seed plants
Division	: Magnoliophyta - Flowering plants
Class	: Magnoliopsida - Dicotyledons
Subclass	: Caryophyllidae
Order	: Caryophyllales
Family	: <i>Basellaceae</i>
Genus	: <i>Anredera</i> Juss.
Species	: <i>Anredera cordifolia</i> (Ten.) Steenis

MORPHOLOGY

Binahong (*Anredera cordifolia* (Ten.) Steenis) is a succulent climbing plant which can grow up to 5 meters long. The root is rhizome with soft-

feeling structure which can be propagated in vegetative and generative form. The stem is cylindrical-shaped with the green-reddish color, soft structure, and looks tangled between the stems. The leaf is singular with bright green color and heart-shaped like, has a very short petiole (subsessile) between 1 to 2 centimeters long, the arrangement is alternate, and the length is 5 to 10 centimeters with the width of 3 to 7 centimeters. The leaf blade is thin and limp, the apex part has a cuspidate structure and the base part has a chordate structure, the margin part is flat, and the surface is soft and smooth. The flower of this plant is a rhizome compound with a long stem and appears on the axillary part of the leaf. There are 2 to 3 millimeters long pedicels and 1.5 to 1.8 millimeters long lanceolate-subulate bracts. The petal part of the flower has a length of 2 to 3 millimeters and has a fragrant aroma with cream-whitish color consisting of five strands. The filaments are narrow-triangular, widely divergent, with a single style shorter than the stamens and clavate, bending outwards near the base (Hidayat & Napitupulu, 2015; PIER, 2013).

DISTRIBUTION

Binahong (*Anredera cordifolia* (Ten.) Steenis) is native to Peru, South America, and then introduced to many countries in many continents, such as Africa, Asia, Europe, North America, and Oceania. According to the CABI official datasheet of Invasive Species Compendium (ISC) (2020), the presence of Binahong has become invasive in some countries, such as Kenya, South Africa, Queensland, New Zealand, Chile, etc. The common name of *Anredera cordifolia* in its distribution to other countries varies, for instance in China it is called “luo kui shu”, in

South Africa it is called “madeira ranker”, in USA it is called “heartleaf madeira vine”, etc.

TRADITIONAL PERSPECTIVE

The leaf of Binahong is usually used by Javanese people in Indonesia as traditional medicine which is believed to have some therapeutic effects to treat several diseases, such as diabetes mellitus, hypertension, asthma, diarrhea, to accelerate wound healing process especially after circumcision operating, and other mild to chronic diseases. Javanese people believe that Binahong leaves are good herbal medicine that can treat any disease and make the body healthy (Yuniarti & Lukiswanto, 2017).

PHYTOCHEMICAL SCREENING

Previous study showed that phytochemical screening has shown secondary metabolites, including phenolic, flavonoid, terpenoid/steroid (triterpenoid and β -sitosterol), alkaloid, and saponin, as shown in “Figure 2” and “Table 1” (Basyuni, Ginting, & Lesmana, 2017). Based on Phenolic Phytochemical Screening “Table 1”, positive reactions to FeCl_3 reagents marked by a black color were observed. FeCl_3 reagent is a particular reagent for phenolic and flavonoid-derived compounds that are phenol derivatives “Table 1”. The existence of flavonoids with a 1% FeCl_3 reagent suggested a color change to black.



Figure 2. TLC chromatogram of the Binahong leaf extract showed that triterpenoid (lupeol) and β -sitosterol corresponded to the standard accordingly (Basyuni, Ginting, and Lesmana, 2017).

Figure 2 displayed the effects of positive steroid or terpenoid outcomes on Liebermann-Burchard reagents marked by blue-greenish coloration and the existence of steroid or terpenoid compounds was demonstrated by positive reactions to Liebermann-Burchard reagents (Basyuni, Ginting, & Lesmana, 2017). In addition, the extract was tested to contain the

steroids and terpenoids group with the TLC procedure (1% CeSO₄) reagent. The findings obtained were positive triterpenoids and β-sitosterol, distinguished by a color difference in the extract that matches the standard colors of triterpenoids and β-sitosterol as seen in “Figure 2”.

Table 1. The results of phytochemical screening of secondary metabolites contained in the Binahong leaf extracts by using particular solvents that are suitable for each metabolite.

Secondary metabolite	Reagents	Signal
Phenolic	FeCl ₃	+++
Steroid/Terpenoid	Liebermann-Burchard	+++
	Lupeol (TLC)	+
	β-sitosterol (TLC)	+
Alkaloid	Bouchardat	-
	Wagner	-
	Mayer	-
	Dragendorff	++
Saponin	Aquades-HCl	+++

(-) : No color changes (negative reaction)

(+) : Color change after few drops of reagent added (positive reaction)

(++) : Color change happened slowly after 1 drop of reagent added (positive reaction)

(+++): Immediate color change after 1 drop of reagent added (positive reaction)

Phytochemical screening of alkaloid showed negative results on Bouchardat, Wagner, and Mayer reagents, but positive towards the Dragendorff reagent, marked by the formation of sediment (Table 1). The phytochemical screening of saponin, steroid, and phenolic showed positive results indicated by the formation of stable froth for 10 minutes with 1 to 10 centimeters in height that was not lost

after the addition of one drop of 2 M HCl (Basyuni, Ginting, & Lesmana, 2017).

ANTIMICROBIAL AND ANTI-INFLAMMATORY ACTIVITIES

Binahong leaf is found to contain secondary metabolites, such as triterpenoid, saponins, alkaloids, flavonoids, phenols, and tannins (Abidin *et al.*, 2017). However, no articles are

found to specify the specific types of each secondary metabolite and its mechanisms of action.

According to Babii *et al.* (2016), tricyclic flavonoid 1 was found to inhibit *Staphylococcus aureus* and *Escherichia coli* cell growth and cause bacteria death by rupture of bacteria membrane. Alkaloids were found to be able to kill bacteria and inhibit the ATP-dependent transport for compounds across bacteria cell membranes (Mabhiza, Chitemerere, & Mukanganyama, 2016). Meanwhile, tannin has been proven to be able to inhibit bacterial growth (Javed, Nawaz, & Munazir, 2020). According to Khan *et al.* (2018), saponins were found to be able to disrupt the bacterial cell membrane permeability, therefore the bacteria would undergo cell lysis and increase the lysosome activity as an antimicrobial immune system.

Binahong leaves extract was also containing oleanolic acid that can act as an anti-inflammatory by significantly inhibit the activation of TNF- α , IL-1 β , IL-6 level, and slightly inhibit Nitric Oxide (NO) which was an inflammatory mediator (Sutrisno *et al.*, 2018; Laksmiawati *et al.*, 2017).

Antimicrobial

Binahong leaves were found to be effective against black-pigmented bacteria, such as *Porphyromonas gingivalis* and *Prevotella intermedia*, that cause chronic periodontitis (Maharani, Puspitawati, & Gunawan, 2018). The test was done through the blank-disk diffusion method with brucella agar to find the inhibitory zone of Binahong leaves. First, the bacterial culture from the periodontitis patient that has been purified and tested with the gram-stain test was placed in petri dishes containing brucella agar, then incubated at 37 °C for 15 minutes.

Whereas, the Binahong leaves infusion was dripped to blank discs that have been labeled according to Binahong leaves infusion concentration then put into the brucella agar surface. This experiment was done twice for each Binahong leaves concentration. Lastly, all petri dishes were incubated at 37 °C for 24 hours. The inhibitory zone results were measured from the clear zones diameter in millimeters and compared to the positive control. From the results, the inhibitory zone from a 100% concentration of Binahong leaves gives similar results of inhibition from drugs that treat periodontitis (Maharani, Puspitawati, & Gunawan, 2018).

Binahong leaves are also reported to be effective against *Aeromonas hydrophila*, which is gram-negative bacteria that causes bacterial infection to freshwater fish. In this experiment, the Binahong leaves were washed and air drained for five days, then the dried leaves were ground using a blender into homogeneous powder and placed in a sealed glass container to avoid direct sunlight exposure. The 50 gram of powder was dissolved in 500 mL of ethanol 96%, covered with aluminum foil, and left for two days along with occasional stirring. After two days, samples were filtered with a cotton swab, then evaporated to gather the concentrated Binahong leaves extract and placed in sealed glass bottles. The antimicrobial activity test was performed by utilizing paper discs in a disk diffusion method where the paper discs were soaked into several different concentrations of Binahong leaf extract (0.2%, 0.4%, 0.6%, and 0.8%) and also into negative control and oxytetracycline (positive control) for 15 minutes. The paper discs were placed on TSA (Trypticase soy agar) media where *Aeromonas hydrophila* culture has been spread and incubated for 24 hours at 37 °C. The results were determined by

measuring the inhibition zone diameter. From the results, all concentrations of Binahong leaves extract were capable of inhibiting *Aeromonas hydrophila* growth with 0.8% extract showed the biggest inhibition zone diameter and 0.2% extract showed the smallest inhibition zone (Basyuni, Ginting, & Lesmana, 2017).

Soap that contains Binahong leaves also shows its antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli*. The test was comparing if the Binahong leaves were able to perform antimicrobial activity better with or without foaming agents. First, Binahong leaves were made into simplicia powder by a maceration method with distilled water. After that, it was filtered and evaporated by a vacuum rotary evaporator. Then, the Binahong soap was prepared by adding different amounts of SLS (Sodium lauryl sulfate). For antibacterial testing, the bacteria liquid was tested by a diffusing method in Mueller Hinton Agar (MHA) media wells, where both bacteria were streaked onto the agar and incubated for 24 hours at 37 °C. Then, each bacteria was suspended in 0.9% NaCl and the solutions were compared with McFarland solution. After that, the liquid soaps were dropped into the wells prepared by using micropipette and incubated 24 hours at 37 °C. The observation was done by measuring the diameter of the inhibition zone (DDH), where the inhibition zone was the clear zone found in the agar. Based on the results, the Binahong leaves extract without SLS showed stronger antimicrobial activity on *Staphylococcus aureus* and *Escherichia coli* than the extract that contains SLS (Setyowati, Nurisah, & Wulandari, 2020).

Anti-inflammatory

Sutrisno, *et al.* (2018) proved that Binahong leaves contain oleanolic acid that inhibits

hemolysis activity to prevent inflammation. The test was started by preparing Binahong ethanolic extract by macerating dried Binahong leaves with ethanol and filtered with filter paper, subsequently the filtrate was condensed with rotary evaporator at 60 °C. Anti-inflammatory activity was tested using Membrane Stabilization (MS) assay, by collecting blood from healthy volunteers that did not use NSAID for 2 weeks prior to the blood collecting day. The blood obtained was made into 10% suspension with an isotonic solution (NaCl 0.9%). Meanwhile, the Binahong leaves extract was mixed with hypotonic solution, phosphate buffer solution (pH 7.4), and HRBC 10% v/v in isotonic solution which made into several concentrations (100, 200, 400, and 800 µg/ml) and incubated for 30 minutes at 37 °C. After incubation, the mixture was centrifuged and its supernatant was taken, followed by measurement using spectrophotometer UV-visible at 560 nm. The Binahong leaves extract was found to decrease the hemolysis rate by 81% with 100 ppm concentration by stabilizing the lysosome membrane to prevent the inflammation process in HRBC, however, the higher Binahong leaves extract concentration showed a decreased stabilizing hemolysis activity ability.

From the experiment by Laksmitawati *et al.* (2017), Binahong leaves extract was also found to be able to inhibit activation of inflammatory mediator, such as TNF- α , IL-1 β , and IL-6 level. The extraction process was done with the maceration technique by using 96% ethanol, then the ethanol was filtered. The waste was re-macerated in triplicate and final extraction products were stored at -20 °C. The anti-inflammatory actions were tested on a lipopolysaccharide-induced murine macrophage cell line or RAW 264.7 which has been grown and tested for their viability. The test was done with

biolegend ELISA kit to test the TNF- α , IL-1 β , IL-6 concentration, while NO concentration was tested by using Abnova Kit. Based on the results, Binahong leaves extract can significantly decrease the viability of RAW 264.7, including the level of TNF- α with 250.3 pg/mL of Binahong extract, IL-1 β with 10 μ g/mL, IL-6 with 10 μ g/mL, and NO with 50 μ g/mL.

Binahong leaf extract gel was also found to be able to decrease IL-6 in gingival crevicular fluid that is found to increase in an inflamed gingival tissue and is involved in the periodontal pathological route. The Binahong leaves were extracted and its extract were processed into gel by combining it with other components, such as glycerin, carbopol, nipagin, nipasol, carbopol, HPMC (Hydroxypropyl Methylcellulose), TEA (Triethanolamine), and aquades. The gel was applied with a syringe into the gingival margin in the gingival pocket area and applied on day-0, day-3, and day-5. Then, on day-7, the gingival crevicular fluid was taken and observed by using ELISA (enzyme-linked immunosorbent assay) procedures. Based on the results, IL-6 level in sulcus fluid decreased significantly and it also proved to be able to improve the periodontal status in the patients (Syahfery *et al.*, 2020).

BURN WOUND HEALING, PERINEAL WOUND HEALING, AND DIABETIC WOUND HEALING

Wounds are conditions where trauma from sharp or blunt objects, temperature changes, chemical, electrical, radiation, or animal bites harm the tissue (Ariani, Loho, & Durry, 2014). People have used Binahong (*Anredera cordifolia* (Ten.) Steenis) as herbal medicine to treat wounds, as well as wounds related to diabetes mellitus condition. Diabetes mellitus is a metabolic disorder characterized by a high blood sugar level in the body due to deficiency of the

insulin hormone (American Diabetes Association, 2011). It is also one of the main causes of wound healing disorder. In individuals with diabetes, diabetic ulcers, open wounds on the surface of the skin, may arise. Once the wound develops, it often stays open for long durations. Bacterial infection may occur rapidly if it is left untreated, leading to more serious conditions. Diabetic gangrene may arise, and it may require amputation (Kurniawan, Carolia, & Pheilia, 2014). The lack or broken part of the tissue between the vulva and the anus with an average size of 4 centimeters is called a perineal wound. Perineal wounds occur generally after the mothers giving birth to their baby. This kind of wound is really prone to infection and may lead to serious complications if left untreated or treated in a wrong manner and unhygienically (Aditia *et al.*, 2017).

There are several chemical ingredients in Binahong leaves, including flavonoids, oleanolic acid, protein, ascorbic acid (Ariani, Loho, & Durry, 2014), tannins, as well as triterpenoid, alkaloid, glycoside, and steroid saponins (Kurniawan, Carolia, & Pheilia, 2014). Binahong leaves also have antimicrobial, anti-inflammatory, anti-parasitic, and anti-fever properties (Aditia *et al.*, 2017). The ascorbic acid content in this plant is crucial for the activation of the prolyl hydroxylase enzyme, which supports the stage of hydroxylation in the formation of collagen so that the wound healing process can be accelerated (Ariani, Loho, & Durry, 2014).

The wound healing properties of the Binahong leaves were tested towards five rabbits having two wounds each on their back. One wound was treated using finely grounded Binahong leaves twice a day, while the other wound left untreated. The results suggested that wounds treated with Binahong leaves generated

more granulation tissue and had a thicker crust compared to the untreated wounds (Ariani, Loho, & Durry, 2014).

The chemical contents of Binahong play a big role in wound healing processes (for all types of wounds explained). Collagen production is promoted by the saponin and ascorbic acid content of Binahong leaves (Ariani, Loho, & Durry, 2014; Kurniawan, Carolia, & Pheilia, 2014). For wound closure and increased tissue epithelialization, type 1 collagen is essential (Kurniawan, Carolia, & Pheilia, 2014). Immediately after the injury, blood fibrillar collagen will trigger platelet aggregation and activation, thus producing variables of chemotaxis that begin the wound healing process. In addition, collagen becomes the basis for a new extracellular matrix, and is accelerating the growth of granulation tissue. Binahong saponin content also plays a role in preventing infection due to wounds (Ariani, Loho, & Durry, 2014).

The mechanism of action of flavonoids is to inhibit the lipid peroxidation process, clean up free radicals, help to stop and slow cell necrosis, and boost vascularity in the wound region (Kurniawan, Carolia, & Pheilia, 2014). The flavonoid content is responsible for the anti-inflammatory, antiseptic, antioxidant, and analgesic properties of the Binahong leaves (Aditia *et al.*, 2017). Lipid peroxidation suppression is assumed to increase the viability of collagen fibrils by raising collagen fibers and vascularity, inhibiting cell damage, and increasing DNA synthesis. Moreover, the alkaloids are also capable of initiating the fibroblasts to go into the wound area. The rising number of fibroblasts makes the process of wound healing quicker (Kurniawan, Carolia, & Pheilia, 2014).

BLOOD PRESSURE-LOWERING AND ANTIHYPERTENSIVE ACTIVITIES

Binahong plant was reported to possess antihypertensive properties with fewer side effects than antihypertensive drugs. Oleanolic acid and ursolic acid found in the ethanolic extract of Binahong leaves are suggested to have antihypertensive effects. They are best extracted with ethanol 95% at 50 °C to obtain the maximum yield (Garmana, Sukandar, & Fidrianny, 2016). Pentacyclic triterpenoid compounds including oleanolic acid and ursolic acid are indicated by five hydrocarbon rings without any heteroatoms. Oleanolic acid mitigates hypertension by the regulation of liver lipid metabolites. Another way for oleanolic acid to treat hypertension and improve blood pressure condition is by downregulating fatty acid synthesis and secretory phospholipase A2 (Zhang *et al.*, 2020).

Ethanolic extract of Binahong leaves showed a similar effect with thiazide diuretic which is an antihypertensive drug. Diuretic drugs work by increasing the urine flow rate. Decrease in venous return and cardiac output impacts the blood pressure by initially lowering it. Then, the cardiac output gradually returns to normal. However, the peripheral resistance will decrease which holds a significant role in reducing blood pressure. Diuretic effects of ethanolic extract of Binahong leaves are observed at a dose of 200 mg/kg after 24 hours of administration. In addition, the ethanolic extract of Binahong leaves is suggested to act as a β -adrenergic receptor antagonist. β -adrenergic receptor antagonists work by blocking the receptor sites for epinephrine and norepinephrine which can increase heart rate and force of contraction. The rise of cardiac output due to stress or during exercise is also decreased by β -adrenergic receptor antagonists. Hence, the ethanolic

extract of Binahong leaves can be utilized as a substitute for antihypertensive drugs (Garmana, Sukandar, & Fidrianny, 2016).

Peripheral resistance such as viscosity and turbulence in blood flow holds a significant role in inducing hypertension. The overproduction of superoxide during oxidative stress could induce the exacerbation of hypertension. Binahong leaves ethanolic extract can reduce the formation of superoxide through its antioxidative properties. Hence, reducing peripheral resistance and mitigating hypertension. Another phytochemical with antioxidative properties found in the ethanolic extract of Binahong leaves are flavonoids. Flavonoids contribute to reducing blood pressure through their antioxidative properties and by inducing vasodilation. The increase in nitric oxide (NO) synthase which increases the level of NO in the circulation of rats has been observed due to the ethanolic extract of Binahong leaves. NO stimulates the formation of cGMP which activates protein kinase G. Protein kinase G increases the absorption of calcium to the muscles and reduces the calcium levels in the cytosol (Garmana, Sukandar, & Fidrianny, 2018). This results in the relaxation of the smooth muscles and vasodilation. Hence, reducing peripheral resistance and mitigating high blood pressure (Garmana, Sukandar, & Fidrianny, 2018).

HYPERLIPIDEMIA, HEART DISEASE, AND CHOLESTEROL-LOWERING ACTIVITY

Binahong not only has functions as antimicrobial, anti-inflammatory, wound healing, and antihypertensive, it is also known to have benefits to treat cardiovascular disease (Lestari, Sukandar, & Fidrianny, 2016). WHO explained that the heart disease, whose risk factors of atherosclerosis, hypertension,

hypercholesterolemia, smoking, and obesity may lead to heart attack and death (Lestari, Sukandar, and Fidrianny, 2016; WHO, 2007). Atherosclerosis can be defined as the condition where the endothelial cells in artery blood vessels are thickened and hardened by fats and cholesterol. Not only coronary heart disease, stroke also may occur when the atherosclerosis happens in the artery towards the brain (Lestari, Sukandar, & Fidrianny, 2016; Medis, Puska, & Norving, 2011).

Lestari, Sukandar, and Fidrianny (2016) have proven that the ethanolic leaf extract of Binahong with the dosages of 50 mg/kg, 100 mg/kg, and 200 mg/kg were able to reduce fat deposits or layers in the endothelial cells, cholesterol, triglycerides, and low-density lipoprotein (LDL) cholesterol levels, but do not affect the high-density lipoprotein (HDL) cholesterol levels. LDL cholesterol might cause damage to endothelial cells by increasing nitric oxide (NO) through endothelial NO synthase (eNOS) (Lestari, Sukandar, & Fidrianny, 2016). Saponin contained in leaves extract of Binahong could suppress cholesterol reabsorption by binding bile acids, creating micelles which make the microvilli on the intestinal epithelial cells surface could not absorb cholesterol inside the micelles and then excreted it through feces (Wahjuni, 2014). Fat metabolism inhibition done by saponin may inhibit lipase enzyme secretion as well, which leads to the diminishing of LDL cholesterol levels and increase of HDL cholesterol level in blood (Kismiati *et al.*, 2020). HDL cholesterol has protection functions to reverse cholesterol transport to the liver, inhibit LDL cholesterol oxidation, and neutralize the atherogenic impact caused by the oxidized LDL cholesterol (Yang *et al.*, 2008; Parthasarathy, 1990). Flavonoids contained in Binahong extract also could suppress the fatty acid synthesis and

lower LDL cholesterol level in the tissue (Kismiati *et al.*, 2020; Ouyang *et al.*, 2016).

Moreover, high reactive oxygen species (ROS) generated from hypercholesterolemia will produce malondialdehyde (MDA) through the oxidation of the membrane cells. MDA, which is the end product of lipid peroxidation, is known to be the marker for free radicals increase and superoxide dismutase (SOD) decrease (Wahjuni, 2014). Binahong extract may counteract the oxidant and antioxidant in the body, where antioxidants contained in the leaf of Binahong may prevent the free radical reaction, then decrease the levels of MDA formation from the lipid peroxidation (Wahjuni, 2014).

CONCLUSION

Binahong leaves (*Anredera cordifolia* (Ten.) Steenis) contain several secondary metabolites, which are triterpenoid, saponins, alkaloids, flavonoids, phenol, tannin, oleanolic acid, protein, β -sitosterol, ursolic acid, and ascorbic acid. The presence of these metabolites was proven through the observation of TLC chromatograms that showed certain color changes correspond to the respective metabolites. The metabolites that exist in Binahong leaves are responsible for the pharmacological effects they performed. These chemical contents contribute to the anti-inflammatory, antimicrobial, wound healing, anti-hypertension, and antihyperlipidemic properties of Binahong leaves. To be specific, the anti-hyperlipidemia effect is obtained from saponins and flavonoids content in the ethanolic extract of Binahong leaves. In addition, the flavonoids also possess other pharmacological effects, namely antiseptic, antioxidant, and analgesic effects, and are capable of promoting wound healing and cleaning up free radicals. The antihypertensive effects of Binahong leaves is

caused by the regulation of lipid metabolites by oleanolic acid, peripheral resistance reduction by antioxidative properties and the dilation of blood vessels by flavonoids. It is important to note that this paper was arranged through literature study and may not be fully complete. Moreover, articles regarding the specific secondary phytochemicals contained in Binahong leaves are also still limited, hence further research on these topics is also suggested. However, this content may support further studies related to the utilization of Binahong leaves as a preventative and therapeutic agent for diseases mentioned.

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