Functional properties of *Anredera cordifolia* (Ten.) Steenis: a review

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Abstract. Binahong is a plant native to Southern America and has been globally distributed through Australia, Africa, USA, New Zealand, and Asia. In Indonesia, it is commonly used as traditional medicine. This paper provides a review addressing functional properties of binahong. Based on the literature studies that have been carried out on several scientific journals, binahong possess functional properties such as antioxidant, antimicrobial, antihyperlipidemic, anti-inflammatory, analgesic, anti-obesity, and antidiabetic. Phytochemical screening results from binahong showed alkaloids, flavonoids, triterpenoid, steroid, phenolic acid, glycoside, tannin, and saponin content.

1. Introduction

*Anredera cordifolia* (Ten.) Steenis is a perennial evergreen climbing vine that grows from fleshy rhizomes. This plant has slender and twined stem about 30 m long, green heart-shaped leaves with a length of 1–15 cm and a width of 0.8–11 cm, small irregular aerial tuber that can growth from 5 mm to 25 cm in diameter, and 3–5 mm greenish white to cream-white flowers [1].

*A. cordifolia* is Southern America native plants and has been globally distributed through Australia, Africa, USA, New Zealand, and Asia. *A. cordifolia*, known as binahong in Indonesia, is commonly used as traditional medicine. Studies carried out in Indonesia, showed that binahong ointments prove to have antimicrobial activity [2] and wound healing [3]. The ointment also can treat hematoma by reducing cell inflammation and increasing fibroblast cells [4]. The gel also aided in healing of burns [5,6]. Binahong extract also proved to have antidiabetic activity by lowering blood glucose levels [7] and anti-obesity [8]. In Africa, the plants were used to treat Sexually Transmitted Disease (STD) [9]. In Latin America, Colombia, it is used to treat diabetes, hyperglycaemia, fracture, and conjunctivitis [10]. In Argentina, its stems were used to treat headache and toothache [11].

Phytochemical screening results from binahong showed alkaloids, flavonoids, triterpenoid, steroid, phenolic acid, glycoside, saponin, and tannin content. Alkaloid (betanidine) and phenolic acid (p-coumaric acid) compounds were found in ethanolic extract of binahong leaves [12]. Flavonoids from the ethyl acetate extract of binahong leaves was identified 3,5,3',4'-tetrahydroxylavone and from ethanol extract was identified as 8-glucopyranosyl-4',5,7-trihydroxyflavone (orientoside) that can be used as antidiabetic [13]. Research conducted by Qiong *et al.* [14] showed that binahong leaves also contain two flavanols and four flavones which were bougracol A, 7-O-methylunonal, 4,7-dihydroxy-5-methoxy-8-methyl-6-formyl-lavane, pectolinaringenin, desmosflavone and demethoxymatteucinol.
Triterpenoid (ursolic acid) and saponins (boussingoside, momordin, and larreagenin) are found in binahong leaves. The purpose of this review is to find scientific proves to claim indigenous knowledge about binahong. As a result, it is important to gather researches related to phytochemical, bioactivity, and toxicity of binahong from scientific research.

2. Antioxidant
Several studies have proven the antioxidant activity in binahong leaves. Study conducted by Djamil, Wahyudi, Wahono, & Hanafi [15] have proven antioxidant activity in the methanol, n-hexane, ethyl acetate, and n-butanol extract of binahong leaves by DPPH assay. The results are shown in Table 1 and the highest antioxidant activity is methanol extract with 53.11 IC$_{50}$.

Table 1. Antioxidant activities of binahong leaves extract.

| Sample                | IC$_{50}$ (μg/mL) |
|-----------------------|-------------------|
| Methanol extract      | 53.11             |
| n-hexane extract      | 256.23            |
| Ethyl acetate extract | 57.96             |
| n-butanol extract     | 132.39            |

From another research by Bahtiar, Utami, & Noor [16], ethanol extract of binahong leaves also proven to have antioxidant activity to prevent kidney injury in Unilateral Ureteral Obstruction (UUO) model rats (Table 2). This experiment is carried out by divided rats into six groups (normal group, positive control group losartan 1.18 mg/kg body weight (BW), binahong leaves extract 75 mg/kg BW, binahong leaves extract 150 mg/kg BW, and binahong leaves extract 300 mg/kg BW) then given losartan and binahong leaves ethanol extract orally on day 14 after UUO treatment. The plasma was examined for the superoxide dismutase (SOD) enzyme activity, catalase enzyme activity, and malondialdehyde (MDA). The results revealed that UUO produced high levels of MDA and low SOD and catalase activity in the negative group. Binahong extracts were found to lower MDA levels while increasing SOD and catalase levels activity. However, there is no information about significant difference among group.

Table 2. Effects of binahong leaves ethanolic extracts on malonaldehyde (MDA), superoxide dismutase (SOD) activity, and catalase activity on Unilateral Ureteral Obstruction (UUO) model rats.

| Groups                         | MDA Concentration | SOD Activity | Catalase Activity |
|--------------------------------|-------------------|--------------|-------------------|
|                                | Average ± SD      | Average ± SD| Average ± SD     |
|                                | (nmol/g)          | (U/mL)       | (nmol/g)          |
| Normal group (Non-UUO model rats) | 0.161 ± 0.009    | 108.38 ± 1.945 | 43.29 ± 3.6      |
| Negative group (UUO model rats) | 0.380 ± 0.003    | 32.50 ± 8.132 | 31.30 ± 7.9      |
| Positive group a                | 0.082 ± 0.006    | 96.00 ± 1.05  | 47.74 ± 5.8      |
| Binahong leaves extract 75 mg/kg body weight | 0.103 ± 0.003    | 81.75 ± 4.21  | 30.41 ± 2.6      |
| Binahong leaves extract 150 mg/kg body weight | 0.198 ± 0.011    | 124.5 ± 5.87  | 40.80 ± 6.9      |
| Binahong leaves extract 300 mg/kg body weight | 0.153 ± 0.051    | 104.75 ± 3.96 | 60.77 ± 14.1     |

*Positive group= Group of rats given losartan 1.18 mg/kg body weight (BW).

3. Antihyperlipidemic
Study conducted by Dwitiyanti & Rorenza, 2021 [17] have proven antihyperlipidemic effects from ethanol extract from binahong leaves. This experiment was carried out orally by divided white rats into
6 groups consisting of normal group, negative group (high fat and sucrose diets), positive group (atorvastatin), dose I group (12.5 mg/kg BW), dose II (25 mg/kg BW), and dose III (50 mg/kg BW). The other group, except for normal group was induced with high-fat and sucrose diet. The blood sample were analysed after 64-day treatment. The application of dose 1, 2, and 3 binahong leaves had the effect of reducing total cholesterol and triglyceride levels in white rats, which were comparable to atorvastatin as positive controls. The results can be seen in Figure 1 and 2 [17]. Flavonoid and alkaloid are suspected to be the phytochemical correspond to this activity [17].

![Figure 1](image1.png)  
**Figure 1.** Cholesterol levels in male white rats before and after treatment.

![Figure 2](image2.png)  
**Figure 2.** Triglyceride levels in male white rats before and after treatment.

4. **Antimicrobial: Antibacterial, Antifungal, and Antivirus**  
Several studies have proven antimicrobial activity of binahong and Ainurrochmah, Ratnasari, & Lisdiana [18] suspected alkaloids, saponins and flavonoids are the phytochemical that correspond to antimicrobial activity. Study conducted by Garmana, Sukandar, & Vidrianny [19] compared Minimum Inhibitory Concentration (MIC) value of *A. cordifolia, C. zedoaria, K. galanga, Z. officinale* and *Morinda citrifolia* ethanol extract against *Bacillus cereus* KTCC 1061, *Bacillus subtilis* KTCC 1021, *Escherichia coli* H7 (O156), *Pseudomonas aeruginosa*, Methicillin-Resistant Coagulase-Negative Staphylococcus (MRCNS), and Methicillin-Sensitive *Staphylococcus aureus* (MSSA) which result can be seen in Table 3 [19]. From the result, we can see that binahong ethanol extracts is the most potential extract to inhibit *Bacillus cereus* KTCC 1061, *Bacillus subtilis* KTCC 1021, *Escherichia coli* H7 (O156), *Pseudomonas aeruginosa*, Methicillin-Resistant Coagulase-Negative Staphylococcus (MRCNS), and Methicillin-Sensitive *Staphylococcus aureus* (MSSA) because it has the lowest MIC compare to *C. zedoaria, K. galanga, Z. officinale* and *Morinda citrifolia* extracts.
Table 3. Antibacterial activity of binahong leaves ethanol extracts.

| Microbes                  | A. cordifolia | C. zedoaria | K. galanga | Z. officinale | Morinda citrifolia |
|---------------------------|---------------|-------------|------------|---------------|-------------------|
| *Bacillus cereus*         | 256           | 1024        | 1024       | 512           | >2048             |
| KTCC 1061                 |               |             |            |               |                   |
| *Bacillus subtilis*       | 256           | 2048        | 2048       | 1024          | 2048              |
| KTCC 1021                 |               |             |            |               |                   |
| *Escherichia coli* H7 (O156) | 256           | 1024        | 2048       | 1024          | 2048              |
| *Pseudomonas aeruginosa*  | 256           | 1024        | 2048       | 128           | 1024              |
| MRCNS<sup>b</sup>         | 512           | 1024        | 2048       | 1024          | 2048              |
| MSSA<sup>c</sup>          | 512           | >2048       | >2048      | 512           | 2048              |

<sup>a</sup> MIC = Minimum Inhibitory Concentration.
<sup>b</sup> MRCNS = Methicillin-Resistant Coagulase-Negative Staphylococcus.
<sup>c</sup> MSSA = Methicillin-Sensitive *Staphylococcus aureus*.

The ethanol extract of binahong leaves had antibacterial activity against *Shigella flexneri* strain BW 1201 with extract concentrations of 0%, 40%, 60%, 80%, and 100% which was indicated by the formation of zones of inhibition. The inhibiting zones of *Shigella flexneri* strain BW 1201 shown in Table 4 [18].

Table 4. The average diameter of inhibiting zones on the growth of *Shigella flexneri* strain BW 1201 with binahong leaves ethanol extract.

| Concentration (%) | Average ± SD (mm) |
|-------------------|-------------------|
| 0                 | 0                 |
| 40                | 18.5 ± 0.95       |
| 60                | 21.2 ± 0.74       |
| 80                | 24.5 ± 0.89       |
| 100               | 27.2 ± 2.18       |

Research by Sudiono, Gunawan, Maharani, & Aipassa [20] has shown that binahong leaves 70% ethanol extract (BLEE) have antifungal activity against *Candida albicans*, fungi that cause oral cavity infection. This study was done by in-vitro with dilution method of BLEE with 0.2%, 0.4%, 0.8%, 1.5%, 3.15%, 6.3%, 12.5%, 25%, 50%, 100% concentration while Nystatin oral suspension and aquadest were used as positive and negative control. The result showed that the lowest colony numbers was found at the concentration of 12.5% BLEE, therefore there were no colonies found at the concentration of 25-100% BLEE while all negative control sample showed colonies growth. There was also no significant difference in *Candida albicans* inhibitory effect between BLEE (12.5–100% concentration) and nystatin oral as the positive control.

Study conducted by Mulaudzi, Ndhlala, & Van Staden [21] have proven the presence of antiviral activity in inhibiting HIV-1 reverse transcriptase (HIV-1 RT) on binahong seeds in phytotherapeutic product. Binahong seeds in phytotherapeutic product was compared to Combivir® and Kaletra® for percent inhibition and IC<sub>50</sub> of HIV-1 RT that were shown in Table 5. The results showed that phytotherapeutic binahong seeds exhibited insignificant and moderate activities against HIV-1 RT compared to Combivir® and Kaletra®.
Table 5. Antiviral activity of binahong seeds against Human Immunodeficiency Virus-1 Reverse Transcriptase (HIV-1 RT).

| HIV-1 RT inhibitory activity (mg/ml) | Inhibition (%) | IC₅₀ (μg/mL) |
|--------------------------------------|----------------|-------------|
| Binahong seeds phytotherapeutic product | 64.41 ± 5.04  | 0.18 ± 0.04 |
| Combivir®                             | 79.80 ± 0.12  | 0.06 ± 0.03 |
| Kaletra®                              | 62.50 ± 0.31  | 0.30 ± 0.10 |

5. Anti-inflammatory

Study conducted by Kurniawan & Carolia [22] proved anti-inflammatory of binahong leaves extract. This study was carried out by divided Sprague Dawley rats with edema into 5 group, aquadest as negative control, 12.6 mg/200 g BW mefenamic acid, 25.2 mg/200 g BW binahong leaves extract, 50.4 mg/200 g BW binahong leaves extract, and 100.8 mg/200 g BW binahong leaves extract. Binahong leaves extract and mefenamic acid were given orally and percent anti-inflammation was calculated. The results can be seen in Table 6. showed that 50.4 mg/200 g BW binahong extract is the best dose with the highest anti-inflammatory, which is 10.12%. At a dose of 100.8 mg/200 g BW, the extract had an anti-inflammatory effect binahong leaves are actually lower compared to a dose of 50.4 mg/200 g BW. This happens because of the possibility that at doses above 50.4 mg/200 g BW an antagonistic effect occurs so that the binahong leaves extract may worsened or even have no effect on anti-inflammation. Although the anti-inflammatory effect of binahong leaves extract was lower than that of mefenamic acid which was used as a positive control, this study has proven pharmacologically that binahong leaves has an anti-inflammatory effect.

Table 6. Effect of binahong leaves extract on anti-inflammation in edema rats.

| Group                                             | Anti-inflammation (%) |
|---------------------------------------------------|-----------------------|
| Negative control (aquadest)                        | 11                    |
| Positive control (mefenamic acid)                  | 5.17                  |
| 25.2 mg/200 g body weight binahong leaves extract  | 10.12                 |
| 50.4 mg/200 g body weight binahong leaves extract  | 1.92                  |

Another study showed that binahong leaves extract ointment has an anti-inflammatory effect in reducing polymorphonuclear neutrophils (PMN) in incision wounds [23]. The study was conducted in vivo on 30 male Sprague Dawley rats which were divided into alkaline groups, povidone iodine, 10% 20% and 40% binahong leaves extract. Rats were given an incision in the back and after 4 hours, blood neutrophil levels were measured. The rats were given ointment according to their groups for 3 days and then the neutrophil levels were measured again. The results of the average neutrophil levels before and after treatment are shown in Table 7. High neutrophil levels before treatment indicate an inflammatory response. After treatment, in negative control group, there were no statistical differences due to p>0.05. Group with 40% binahong leaves extract ointment is the group with the best dose because it has the greatest decrease in neutrophil levels. Susanti [23] also suspected that flavonoid is the phytochemical that correspond to anti-inflammatory activity.

Table 7. Average neutrophil levels before and after treatment in rats with binahong leaves extract ointment.

| Groups                                | Average ± SD (%) | p  |
|---------------------------------------|------------------|----|
| Negative control (base ointment)      | 40.67 ± 4.80     |    |
|                                       | 35.33 ± 5.95     |    | 0.08 |
6. Analgesic

Yuziani, Harahap, & Karsono [24] stated that flavonoids and triterpene are phytochemicals that correspond to analgesic activity. Yuziani, Harahap, & Karsono [24] also proven that ethanol extract of binahong leaves at doses of 100, 200, and 400 mg/kg BW have analgesic effect on Wistar albino rats [24]. The study was used Plantar test where five groups of rats were treated orally with ethanolic extract (100, 200, and 400 mg/kg BW), 2.25 mg/kg sodium diclofenac (positive control) and CMC-sodium 1% (negative control) and the reaction of latency for licking hind paw or jumping noted at 10, 20, 30, 40, 50, and 60 minutes post treatment. The results showed that time to feel early pain was longer than negative control group that can be seen in Table 8. Extract dosages of 400 mg/kg BW binahong leaves ethanolic extract gave the greatest analgesic response and had a significant analgesic effect that was comparable to the positive control, sodium diclofenac.

| Group | Initial Pain Relief (s) |
|-------|-------------------------|
|       | 10          | 20          | 30          | 40          | 50          | 60          |
| Negative control  | 3.92 ± 2.05 | 5.17 ± 1.87 | 4.34 ± 2.12 | 5.37 ± 2.12 | 6.63 ± 1.87 | 5.12 ± 1.87 |
| (CMC-sodium 1%)   | 1.05 ± 0.87  | 2.21 ± 1.12 | 0.56 ± 0.23 | 1.27 ± 0.27 | 1.88 ± 0.27 | 2.05 ± 0.27 |
| Positive control  | 11.58 ± 2.56 | 15.48 ± 2.34| 17.97 ± 3.26| 25.56 ± 3.26| 28.30 ± 3.26| 36.22 ± 3.26|
| (Sodium diclofenac 2.25 mg/kg) | 2.82 ± 0.87 | 4.06 ± 1.12 | 3.33 ± 0.23 | 2.60 ± 0.27 | 1.03 ± 0.27 | 1.81 ± 0.27 |
| 100 mg/kg body weight (BW) | 9.33 ± 2.05 | 14.32 ± 2.34| 17.60 ± 3.26| 19.72 ± 3.26| 21.22 ± 3.26| 25.17 ± 3.26|
| binahong leaves  | 2.16 ± 0.87  | 3.12 ± 1.12 | 4.23 ± 0.23 | 5.28 ± 0.27 | 4.05 ± 0.27 | 2.50 ± 0.27 |
| 200 mg/kg body weight (BW) | 13.30 ± 2.05 | 17.98 ± 2.34| 17.67 ± 3.26| 21.67 ± 3.26| 25.27 ± 3.26| 30.18 ± 3.26|
| binahong leaves  | 2.82 ± 0.87  | 3.03 ± 1.12 | 4.97 ± 0.23 | 2.65 ± 0.27 | 4.10 ± 0.27 | 4.15 ± 0.27 |
| 400 mg/kg body weight (BW) | 10.25 ± 2.05 | 12.28 ± 2.34| 20.08 ± 3.26| 26.82 ± 3.26| 31.03 ± 3.26| 35.10 ± 3.26|
| binahong leaves  | 3.84 ± 0.87  | 2.07 ± 1.12 | 5.45 ± 0.23 | 2.57 ± 0.27 | 4.55 ± 0.27 | 3.90 ± 0.27 |

Water extract of binahong leaves at doses of 50, 100, and 200 mg/kg bw were given orally to male Swiss Webster mice and proven to give analgesic effect [25]. Analgesic activity from binahong leaves water extract was observed from the decrease of total writhing and percent protection compared to CMC 0.5% as the control group every 10 min for 1 h and compared with 65 kg/mg BW aspirin. The results are shown in Table 9 [25]. The total amount of writing experienced by mice in the water extract group with dosages of 50 mg/kg BW, 100 mg/kg BW, and 200 mg/kg BW was considerably lower than in the control group. The findings also revealed that increasing doses resulted in increased analgesic activity. The analgetic activity of water extract doses of 100 mg/kg bw and 200 mg/kg bw were statistically show no significant difference compared to aspirin, means that analgesic activity of 100 and 200 mg/kg BW binahong leaves water extract was comparable to aspirin.

| Group                   | Dose (mg/kg body weight) | Total Writhing | Protection (%) |
|-------------------------|--------------------------|----------------|----------------|
| Control group (CMC 0.5%)| 10                       | 86.80 ± 29.80  |                |
| Aspirin                 | 65                       | 21.00 ± 23.21  | 75.81          |
| Binahong leaves water   | 50                       | 55.20 ± 24.24  | 36.41          |
|                         | 100                      | 29.60 ± 13.45  | 65.90          |
7. Anti-obesity

Binahong leaves proven to have anti-obesity activity and saponin is suspected correspond to anti-obesity [8]. Study conducted by Sukandar, Kurniati, & Nurdianti [8] on healthy adult male Wistar rats prove the anti-obesity activity of ethanol extract binahong leaves by attenuate the body weight increment. The rats were divided into four groups: positive control, ethanol extract of binahong leaves at 50 and 100 mg/kg BW, and Orlistat at 21.6 mg/kg BW. All rats in groups were fed a high-carbohydrate diet for 30 days. The rats were treated orally for 14 days based on their groups after 30 days, and the high-carbohydrate diet was continued throughout the treatment. The effect of each treatment on rat body weight can be seen in Table 10 [8]. Ethanol extract of binahong leaves at a dose of 100 mg/kg BW showed the best effect in inhibiting the increment of body weight which was significantly different compared to positive control. Anti-obesity activity of 100 mg/kg BW ethanol extract binahong leaves also better compared to 21.6 mg/kg BW Orlistat.

| Groups | Body weight increment at day of treatment (%) |
|--------|---------------------------------------------|
|        | 3   | 7   | 10  | 14  |
| Negative control (non-obese rats) | 47.78 ± 6.26 | 55.23 ± 7.34 | 58.85 ± 7.89 | 67.56 ± 8.21 |
| Positive control (obese rats) | 56.31 ± 5.29 | 64.40 ± 6.73 | 69.44 ± 7.26 | 76.11 ± 8.50 |
| 50 mg/kg body weight binahong leaves | 54.53 ± 4.92 | 60.86 ± 4.99 | 65.73 ± 4.02 | 72.76 ± 5.16 |
| 100 mg/kg body weight binahong leaves | 49.88 ± 6.83 | 56.50 ± 4.67 | 58.06 ± 5.78 | 59.97 ± 5.63 |
| 21.6 mg/kg body weight Orlistat | 52.57 ± 9.93 | 61.37 ± 10.89 | 64.88 ± 11.51 | 65.46 ± 12.80 |

*a Significant difference compared to positive control group, p<0.05.

8. Antidiabetic

Djamil, Winarti, Zaidan, & Abdillah [26] proved that the flavonoid compound, orietoside, has antidiabetic activity in alloxan-induced mice. Mice were divided into 5 groups, which were made diabetic with 250 mg/kg BW of alloxan received 0.5 ml distilled water, 40 mg/100g of acarbose, 10, 50 and 100 mg/kg BW of orietoside, orally, respectively. The antidiabetic activity of orietoside results is shown in Table 11 where only the dosage 100 mg/kg BW orietoside for 14 days could decrease the blood glucose concentration to the same levels as the normal group and acarbose (p<0.05).

| Group | Fasting blood sugar level (mg/dL) |
|-------|----------------------------------|
|       | At the time of grouping | Days of active compounds supplementation |
|       | 0   | 7   | 14  |
| Diabetic | 234 ± 45 | 232 ± 67 | 226 ± 68 | 219 ± 154 |
| 10 mg/kg body weight of vitexin | 267 ± 78 | 245 ± 87 | 236 ± 78 | 223 ± 120 |
| 50 mg/kg body weight of vitexin | 309 ± 110 | 305 ± 138 | 301 ± 121 | 186 ± 119 |
| 100 mg/kg body weight of vitexin | 260 ± 82 | 250 ± 59 | 103 ± 87 | 80 ± 21 |
According to the study conducted by Sukandar, Qowiyyah, & Larasari [27], methanol extract of binahong leaves also have antidiabetic activity. This study was carried out by given binahong extract orally to Swiss Webster mice that was induced by alloxan for 14 days and measured the blood glucose level. The results can be seen in Table 12 and 13. On days 7 and 14, the results demonstrated that a methanol extract of binahong leaves at doses of 50, 100, and 200 mg/kg BW significantly reduced blood glucose levels compared to the positive control group.

### Table 12. Average blood glucose levels of mice before and after being given binahong leaves methanol extract.

| Group                     | Blood glucose level (mg/dL) on the day of observation |
|---------------------------|-----------------------------------------------------|
|                           | 0         | 1         | 7         | 14        |
| Positive control          | 282.0 ± 114.4 | 328.8 ± 124.3 | 256.6 ± 141.4 | 259.6 ± 172.5 |
| 0.65 mm/kg body weight glibenclamide | 314.9 ± 107.2 | 103.6 ± 13.8 | 86.0 ± 26.1 | 74.4 ± 31.4 |
| 50 mm/kg body weight binahong extract | 328.4 ± 85.5 | 178.6 ± 31.2 | 128.0 ± 55.6 | 80.0 ± 25.8 |
| 100 mm/kg body weight binahong extract | 397.0 ± 84.3 | 309.0 ± 101.2 | 303.0 ± 140.0 | 200.0 ± 58.0 |
| 200 mm/kg body weight binahong extract | 259.4 ± 114.9 | 257.4 ± 120.1 | 102.0 ± 63.3 | 86.6 ± 25.3 |

### Table 13. Percentage of decreased blood glucose levels in male diabetes alloxan by the effect of giving binahong leaves methanol extract.

| Group                     | The percentage decrease in blood glucose levels on the day of observation |
|---------------------------|-------------------------------------------------------------------------|
|                           | 1         | 7         | 14        |
| Positive control          | -145.32\(^a\) | 9.0       | 7.94      |
| 0.65 mm/kg body weight glibenclamide | 67.0       | 72.61     | 76.30     |
| 50 mm/kg body weight binahong extract | 45.61     | 61.02     | 75.64     |
| 100 mm/kg body weight binahong extract | 22.17     | 23.68     | 49.62     |
| 200 mm/kg body weight binahong extract | 0.77      | 60.68     | 66.61     |

\(^a\) - indicates increasing blood glucose levels.

### 9. Toxicity

Salasanti, Sukandar, & Fidrianny [28] conducted study about acute and sub chronic toxicity of ethanol extract binahong leaves on ddY mice. The acute toxicity study was carried out by given binahong leaves ethanol extract orally at dose ranging between 0.05-15 g/kg BW. The animals were monitored for 14 days during any changes in activity such as excitation, fatigue, diarrhoea, itching, warping tail, shivering, hair loss and death. Sub chronic toxicity study was carried out by given binahong extract orally at doses of 0.1 g/kg BW, 0.4 g/kg BW, and 1 g/kg BW for 90 days and behaviour, mortality, and body weight were observed during study period. At the end of period, relative organ weight, haematology, blood biochemistry, and histopathology were observed. The results are no mortality at acute toxicity test even at highest dose of 15 g/kg BW. In sub chronic toxicity test, the results are no mortality, no significantly differences in body weight, organ weight, haematology, and blood biochemistry and the histology observations also showed no different of heart, lung, liver, kidney and spleen with the control group at concentration up to 1 g/kg BW binahong leaves ethanol extract.

Wijayanti, Kurnianto, & Setiatin [29] conducted study about toxicity effect of binahong leaves methanol extract in liver of guinea pigs (Cavia cobaya). The study was carried out by given binahong
leaves extract orally to guinea pig at dose of 0, 10, 50, and 90 mg/head for 10 days. At the 11th day, liver were taken to histopathology and toxicity test. Damage to hepatocyte were examined with conditions such as damage I (albuminose degeneration), damage II (hydropic degeneration), damage III (fat degeneration), and damage IV (necrosis). At dose of 0 mg/head, there is a presence of albuminose degeneration. This indicates that guinea pig had suffered from infection/disorders before treatment. At dose of 10, 50, and 90 mg/head binahong leaves extract, there are hydropic degeneration in the liver. Of all treatments, there were no deaths in guinea pig. The weight of the liver who was given 10, 50, and 90 mg/head binahong leaves extract were lighter than 0 mg/head. It is because binahong contains flavonoid that keep warding off toxins. Overall, binahong leaves extract up to 90 mg/head had no significance toxicity effect on guinea pigs’ liver.

Discussion
Activities that found in binahong leaves are antioxidant, antibacterial and fungal, antihyperlipidemic, anti-inflammatory, analgesic, anti-obesity, and antidiabetic. Antiviral was conducted on binahong seeds. Among those activities, antioxidant, antihyperlipidemic, antimicrobial, analgesic, and anti-obesity are from ethanol extract while analgesic from water extract and antidiabetic from methanol extract. Phytochemical compound that corresponds to these activities are flavonoid, phenolic acid, saponin, alkaloid, triterpenes, and steroid. Flavonoid and phenolic acid are phytochemical that play a role in antioxidants by ward off the free radicals [30,31].

Hyperlipidemic is a condition where there is increasing in total cholesterol, low density lipoprotein (LDL), triglycerides, and a decrease in high density lipoprotein (HDL) [17]. Flavonoid, alkaloid, phenolic acid, and saponin are suspected for anti-hyperlipidaemic because it can reduce total cholesterol and increase HDL concentration [17]. For antimicrobial activity, alkaloids, saponins and flavonoids may possess this activity [18]. The mechanism of inhibition is by destroying the peptidoglycan components of bacterial cells, so the cell wall layer is not fully formed. Damage to the cell wall causes the permeability of the cell membrane to change and will inhibit the work of intracellular enzymes and causing the entry of water uncontrolled into bacterial cells which ultimately results in death [18].

Anti-inflammation activity occur due to flavonoid, alkaloid, and triterpene and analgesic activity are due to flavonoid and triterpene [24]. Those works by inhibiting the cyclooxygenase enzyme (COX) and reducing prostaglandin production by arachidonic acid to alleviate pain, as well as decreasing neutrophil degranulation to minimize the generation of cytokines, free radicals, and enzymes involved in inflammation [22,24]. Both flavonoid and saponin correspond to anti-obesity and antidiabetic activity by inhibit postprandial elevation of the blood glucose level that promotes lipid accumulation and also inhibit fats absorption [32,33]. Binahong administration in rats should not exceed 50 mg/200 g BW orally, because it can cause antagonistic effects.

Conclusion
Binahong extract showed a promising bioactivity for antioxidant, antihyperlipidemic, antimicrobial (antibacterial, antifungal, and antiviral), anti-inflammatory, analgesic, antiobesity, and antidiabetic activities. Binahong also showed no toxic signs or abnormalities, so it can be considered to be safe for medicinal uses. However, research on this activity is still carried out in vitro and in vivo (via mice), so the ability in the human body still needs to be analyzed further.

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