Antimicrobial and Antioxidant Medicinal Plants in Kwau Village and Silau Village, Warmare District, Manokwari District, West Papua

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ABSTRACT
The purpose of this study was to evaluate antimicrobial and antioxidant of medicinal plants in the villages of Kwau and Siau (Phytochemical, antioxidant, anti-bacterial, antifungal, and toxicity). The bark, roots, and leaves are extracted with methanol to get the extract. Antimicrobial activity against Propionibacterium acnes, Escherichia coli, Streptococcus sobrinus, and Candida albicans was determined by a good diffusion method. The DPPH radical scavenging activity mechanism assayed antioxidant activity. Antimicrobial activity against the bacteria and fungi was determined by the agar well diffusion method. Antioxidant activity was tested by DPPH radical rinsing activity mechanism. Toxicity was determined by the Brine Shrimp Lethality Test method. The results showed that methanol extract showed good activity against acne in only 8 of 13 species, ten species of 13 species for E.colii, three species of 13 species for S. sobrinus and, ten species of 13 species for C. albicans at 25-500 ppm of extract tested. The toxicity test showed that 0% of the deaths from Artemia salina Leach shrimp indicated that the absence of harmful compounds was toxic in the sample, meaning that it was very safe to be consumed directly by humans, except for the roots of Spondias cytherea Senn and the bark of Inocarpus fragiferua Fosk.

Keywords: Antimicrobial activity, Antioxidant activity, Citotoxicity assay, Phytochemical analysis

1. INTRODUCTION
Papua has considerable forest resource potential, both in terms of broad aspects and type of forest. Diversity of flora between 16,000 and 20,000 species. At least 124 genera of endemic flowering plants in Papua [1]. Papua Province has a wide variety of biological resources, so that Papua is the richest concentration area in Indonesia. In its use, traditional medicine is more often used by the people of Papua because it is believed to have the ability to heal better than modern medicine and the side effects it causes are mild [2]. The number of medicinal plants in Papua causes almost most Papuans to be more likely to use traditional medicine than modern medicine because it is easily available. The amount is still widely available in the world. According to the Papuan people, knowledge of traditional medicine has been passed down through generations from generation to generation. So that the Papuan people, especially the indigenous people, do not use modern medicine in treatment. This has led to the need for research to find out the chemicals contained in medicinal plants. Kwau and Siau villages in Wamare district are remote areas. Still, they use many medicinal plants as treatment needs, so there is a need for research on phytochemicals and their biological activities such as anti-bacterial, antifungal, and toxicity of the medicinal plants.

2. MATERIALS AND METHODS

2.1. Plant materials and chemicals

The research material came from the Kwau and Siau Villages, analyzed in the forest technology laboratory of the Unipa Manokwari Forestry Faculty and the Wood Technology Laboratory, Faculty of Forestry, Mulawarman University, Samarinda. The plant materials were shade dried for three days and ground with a blender. DPPH (1,1-diphenyl-2-picrylhydrazyl) was purchased from Tokyo Kasei Kogyo (Tokyo,
2.2. Extraction

The extraction method used is maceration using methanol. The macerated sample depends on the amount obtained from the field (varies). The sample is dissolved with methanol with a ratio of 1:4. Maceration was carried out for ± 3 days then filtered with a Buchner funnel. The maceration results were concentrated or evaporated using a rotary vacuum evaporator at a temperature of 40°C and then stored in a vacuum oven until a crude extract was obtained. The yield of the extraction showing in Table 1.

2.3. Antimicrobial assay

Propionibacterium acnes, Escherichia coli, Streptococcus sobrinus, and Candida albicans were used in all experiments. Nutrient agar and potato dextrose agar were used in anti-bacterial and antifungal assays, respectively. Plant extracts were dissolved in acetone to obtain a concentration of 125, 250, and 500 μg/1000 μg, which was selected based on our preliminary results showing the antimicrobial activity of plant extract tested simultaneously correlates with the concentration of standard drugs used (20 μg/disk). Antimicrobial assays were conducted using the disc diffusion method as previously described by Kusuma et al. 2011 [3]. Zones of inhibition around the discs were measured in mm. Activity index (AI) was calculated as the mean inhibition zone for the test sample divided by the mean inhibition zone for the standard [4].

2.4. Antioxidant assay

The sample was first dissolved in DMSO and used at a 30 times dilution for the actual experiment. The DPPH radical scavenging method was performed as previously described by Arung et al. 2011. UV absorption was measured on a Shimadzu UV-VIS 1200 spectrophotometer (Shimadzu Corp., Kyoto, Japan).

2.5. Cytotoxicity assay

According to the method described in [5], the cytotoxicity assay was performed using the brine shrimp lethality test. Analysis of the data was performed by probit analysis on a computer program to determine LC50.

2.6. Phytochemical analysis

One gram of the plant ethanol extracts was dissolved in 100 mL ethanol and subjected to preliminary phytochemical screening following standard methods [6, 7, 8].

3. RESULTS AND DISCUSSION

3.1. Phytochemical

Leaves, skin, sap, roots, and stems of medicinal plants in the Arfak Mountains macerated with methanol produced 3.11% - 25.58% extract based on the sample dry weight shown in Table 1. Leaves Ficus cf. anulata Blume gives the lowest yield, while Calophyllum peekeli Luterb leaves produce the highest extract. This can be caused by solvents that are polar types to dissolve more components of the plant extracts' metabolite compounds. The high and low yields depend on the type of solvent used; the more polar the solvent will be, the higher yield produced [9,10,11].

Phytochemical analysis of plant extracts in Siau and Kwau villages in the Manokwari District showed alkaloids, flavonoids, saponins, tannins, triterpenoids, steroids, carotenoids, and coumarin (Table 2). The most common component is flavonoids, followed by tannins and coumarins, the least of which are coumarin, steroids, and saponins. Flavonoids in plants generally function as growth regulators, photosynthetic regulators, antimicrobial and antiviral work. Flavonoids are natural antioxidants where flavonoids can change or reduce free radicals and as anti-free radicals. Flavonoid compounds have been proven to be very instrumental in the field of medicine [12].

3.2. Antioxidant

The DPPH radical mechanism evaluated the antioxidant activity of plant extracts. DPPH is a free radiological compound that has been widely used to test free radicals' ability from various types of samples [13]. This method is often used because it is simple, easy, fast, and sensitive and only requires a few samples. Antioxidant compounds react with DPPH radicals through a hydrogen atom donation mechanism and cause DPPH colour decay from purple to yellow [14]. The results are shown as activity relative to standard ascorbic acid [13]. Antioxidant activities of medicinal plants in the Manokwari district can be seen in Table 3. The lowest percentage of DPPH absorption ranged from 29 - 74% in the highest Spondias cytherea Senn in Coffea Arabica L. Medicinal plants in the Kwau and Siau villages of Manokwari Regency are antioxidants, from the results of phytochemical analysis of medicinal plants in Manokwari Regency containing saponins, tannins, and carotenoids. Saponins, tannins, and carotenoids are sources of antioxidants. Six types are...
Table 1. Rendemen of medicinal plants in the villages of Kwau and Siau, Manokwari Regency

| No. | Local Name     | Latin name                      | Parts of used | Weight of sample (g) | Weight of extract (g) | Percentage (%) |
|-----|----------------|---------------------------------|---------------|----------------------|-----------------------|----------------|
| 1   | Amihou Kwau    | *Spondias cytherea* Senn.       | Leaves        | 188.8744             | 27.9022               | 14.77          |
| 2   | Bikibea Kwau   | *Ficus cf. anulata* Blume       | bark          | 261.3728             | 10.4216               | 3.99           |
| 3   | Bipasyomkwau   | *Calophyllum peekeli* Luterb    | Leaves        | 434.7983             | 111.2396              | 25.58          |
| 4   | Ciga           | *Pongamia Pinnata* (L.) Pierre  | bark          | 308.3025             | 15.7556               | 5.11           |
| 5   | Kopi           | *Coffea arabica* L.             | Leaves        | 107.2548             | 5.6320                | 5.25           |
| 6   | Daun sirsak    | *Annona muricapa* L.            | Leaves        | 166.0977             | 11.9870               | 7.22           |
| 7   | Musromah siau  | *Homalanthus* sp.               | Leaves        | 51.9213              | 2.1722                | 4.18           |
| 8   | Giniua Kwau    | *Saurauia* sp.                  | bark          | 236.5198             | 13.6885               | 5.79           |
| 9   | Jetroga soub   | *Hydnopictum* sp.               | root          | 562.5642             | 97.9554               | 17.41          |
| 10  | Tisia Kwau     | *Sida acuta* Burm.f.            | Leaves        | 125.5273             | 8.6340                | 6.88           |
| 11  | Kikar          | *Inocarpus fragiferua* Fosk     | Leaves        | 190.3915             | 5.9266                | 3.11           |
| 12  | Komka mef      | *Pimelodendron* amboinicum (Hassk.) Miq. | bark | 680.0784             | 26.3412               | 3.87           |
| 13  | Kama Kwau      | *Thibaudia* sp.                 | Leaves        | 323.2423             | 23.9725               | 7.42           |

Table 2. Phytochemical composition of medicinal plants in the villages of Kwau and Siau, Manokwari Regency

| No | Local Name     | Latin Name                      | part of used | Alk | Flav | Sap | Tan | Trip | Ste | Kar | Kum |
|----|----------------|---------------------------------|--------------|-----|------|-----|-----|------|-----|-----|-----|
| 1  | Amihou Kwau    | *Spondias cytherea* Senn.       | leaves       | -   | -    | -   | +   | +    | -   | +   | -   |
| 2  | Bikibea Kwau   | *Ficus cf. anulata* Blume       | Barks        | +   | -    | +   | -   | +    | -   | -   | -   |
| 3  | Bipasyomkwau   | *Calophyllum peekeli* Luterb    | leaves       | -   | -    | +   | -   | -    | -   | -   | -   |
| 4  | Ciga           | *Pongamia Pinnata* (L.) Pierre  | barks        | -   | -    | -   | +   | -    | -   | +   | -   |
| 5  | Kopi           | *Coffea arabica* L.             | leaves       | -   | +    | -   | -   | -    | -   | -   | -   |
| 6  | Sirsak         | *Annona muricapa* L.            | leaves       | -   | +    | +   | -   | +    | -   | -   | -   |
| 7  | Musromah Siau  | *Homalanthus* sp.               | leaves       | +   | -    | -   | -   | +    | -   | -   | -   |
| 8  | Giniua Kwau    | *Saurauia* sp.                  | barks        | +   | -    | -   | -   | +    | -   | -   | -   |
| 9  | Jetroga soub   | *Hydnopictum* sp.               | roots        | +   | -    | -   | -   | -    | -   | -   | -   |
| 10 | Tisia Kwau     | *Sida acuta* Burm.f.            | leaves       | -   | +    | -   | -   | +    | +   | -   | -   |
| 11 | Kikar          | *Inocarpus fragiferua* Fosk     | leaves       | -   | +    | -   | -   | +    | +   | +   | +   |
| 12 | Komka mef      | *Pimelodendron* amboinicum (Hassk.) Miq. | barks  | +   | +    | -   | -   | +    | -   | -   | -   |
| 13 | Kama Kwau      | *Thibaudia* sp.                 | leaves       | -   | +    | -   | -   | -    | -   | -   | +   |

very powerful antioxidants (*Ficus cf. Blume anulata*, *Pongamia pinnata* (L), *Coffea Arabica* L, *Annona muricapa* L, and *Homalanthus* sp).

3.3. Anti-Bacteria Propionibacterium acne

With the agar diffusion method, the anti-bacterial extract was carried out against *Propionibacterium acne* bacteria. A positive result if an inhibition zone is formed around the well. After incubating for 24 hours at 37°C, the results were seen by comparing the extract with positive control. The observations of wells containing extracts of medicinal plants in the Kwau and Siau villages of the Manokwari Regency showed positive results with forming an inhibitory zone around the wells. Of the three repetitions with each of the three wells, the results obtained can be seen in Table 4. Of the 13 types of plants researched, there are two types of anti-bacterial *Propionibacterium acne* strong, six
medium types, two weak types and three types are plants that cannot inhibit the growth of *Propionibacterium acne* bacteria. Table 4. shows that medicinal plants in the Kwau and Siau villages of the Manokwari Regency have different inhibitory effects on *Propionibacterium acne* bacteria. Secondary metabolite compounds in medicinal plants in the Kwau and Siau villages of Manokwari Regency are alkaloids, flavonoids, steroids, tannins, saponins, triterpenoids, carotenoids, and coumarin. The presence of secondary metabolites in various medicinal plants causes different inhibitory forces. Therefore the inhibitory power varies from weak to very strong.

The types of plants with strong inhibitory power have secondary metabolite content in flavonoids, saponins, tannins, and triterpenoids. Tannin has an antibacterial activity related to its ability to activate the adhesion of microbial cells and inactivating enzymes, and disrupting protein transport in the inner layer of cells [15]. The mechanism of flavonoids as antibacterial is to form complex compounds with extracellular and dissolved proteins that can damage the bacterial cell membrane and are followed by the release of intracellular compounds [16]. Terpenoid compounds are also known to be active against bacteria, but the anti-bacterial triterpenoid mechanism is still unknown. The terpenoid anti-bacterial activity is thought to

### Table 3. Activity of Antioxidant of Medicinal Plants in Kwau and Siau Villages, Manokwari Regency

| No | Local Name | Latin Name            | Parts of Used | Rend. extract (%) | Concentration (ppm) | Average replication % | % DPPH inhibition | IC50 |
|----|------------|-----------------------|---------------|-------------------|---------------------|------------------------|-------------------|------|
|    | Vitamin C  |                       |               |                   |                     |                        |                   |      |
| 1  | Amihou     | *Spondias cytherea* Senn. | Leaves       | 14.77             | 100                 | 0.012                  | 96.25             | 15   |
|    |            |                       |               |                   | 50                  | 0.013                  | 95.95             |      |
|    |            |                       |               |                   | 25                  | 0.030                  | 90.88             |      |
| 2  | Bikibeia   | *Ficus cf. anulata* Blume | Barks        | 3.99              | 100                 | 0.204                  | 21.99             | 156  |
|    |            |                       |               |                   | 50                  | 0.241                  | 26.85             |      |
|    |            |                       |               |                   | 25                  | 0.257                  | 37.99             |      |
| 3  | Bipasyom   | *Calophyllum peekeli* Luterb | Leaves      | 25.58             | 100                 | 0.086                  | 73.86             | 225  |
|    |            |                       |               |                   | 50                  | 0.104                  | 68.39             |      |
|    |            |                       |               |                   | 25                  | 0.116                  | 64.84             |      |
| 4  | Ciga       | *Pongamia Pinnata* (L.) Pierre | Barks      | 5.11              | 100                 | 0.082                  | 69.10             | 20   |
|    |            |                       |               |                   | 50                  | 0.093                  | 71.83             |      |
|    |            |                       |               |                   | 25                  | 0.102                  | 75.18             |      |
| 5  | Kopi       | *Coffea arabica* L. | Leaves       | 5.25              | 100                 | 0.039                  | 88.15             | 24   |
|    |            |                       |               |                   | 50                  | 0.052                  | 84.09             |      |
|    |            |                       |               |                   | 25                  | 0.164                  | 50.25             |      |
| 6  | Sirsak     | *Annona muricapa* L | Leaves       | 7.22              | 100                 | 0.071                  | 58.87             | 19   |
|    |            |                       |               |                   | 50                  | 0.080                  | 75.79             |      |
|    |            |                       |               |                   | 25                  | 0.135                  | 78.32             |      |
| 7  | Musromah   | *Homolanthus* sp.     | Leaves       | 4.18              | 100                 | 0.033                  | 52.79             | 9    |
|    | Siau       |                       |               |                   | 50                  | 0.078                  | 76.39             |      |
|    |            |                       |               |                   | 25                  | 0.155                  | 89.87             |      |
| 8  | Gnuia      | *Saurauia* sp.        | Barks        | 5.79              | 100                 | 0.129                  | 76.39             | 85   |
|    |            |                       |               |                   | 50                  | 0.136                  | 52.79             |      |
|    |            |                       |               |                   | 25                  | 0.176                  | 60.69             |      |
| 9  | Jetgora    | *Hydnopictum* sp.     | Roots        | 17.41             | 100                 | 0.324                  | 1.52              | 80   |
|    | Soah Pohon |                       |               |                   | 50                  | 0.253                  | 23.00             |      |
|    |            |                       |               |                   | 25                  | 0.105                  | 68.09             |      |
| 10 | Tisia      | *Sida acuta* Burm.f.  | Leaves       | 6.88              | 100                 | 0.172                  | 47.82             | 117  |
|    |            |                       |               |                   | 50                  | 0.084                  | 74.57             |      |
|    |            |                       |               |                   | 100                 | 0.086                  | 69.40             |      |
| 11 | Kikar      | *Inocarpus fragiferua* Fosk | Leaves    | 3.11              | 100                 | 0.172                  | 47.82             | 117  |
|    |            |                       |               |                   | 50                  | 0.129                  | 60.79             |      |
|    |            |                       |               |                   | 25                  | 0.083                  | 74.77             |      |
| 12 | Komka Mef  | *Pinelodendron amboinicum* (Hassk.) Miq. | Barks  | 3.87              | 100                 | 0.188                  | 62.82             | 75   |
|    |            |                       |               |                   | 50                  | 0.138                  | 58.16             |      |
|    |            |                       |               |                   | 25                  | 0.122                  | 42.96             |      |
| 13 | Kama       | *Thibaudia* sp.       | Leaves       | 7.42              | 100                 | 0.283                  | 14.08             | 83   |
|    |            |                       |               |                   | 50                  | 0.217                  | 34.04             |      |
|    |            |                       |               |                   | 25                  | 0.137                  | 58.46             |      |
increased permeability or leakage of cells

Table 4. Inhibitory Power of Medicinal Plants in Kwau and Siau Villages in Manokwari Regency as Anti-Bacteria of Propionibacterium acne

| No | Local Name | Latin Name | Parts of used | Concent. (µg/well) | replication 1 | replication 2 | replication 3 | mean (mm) | % |
|----|------------|------------|---------------|-------------------|---------------|---------------|---------------|-----------|---|
| 1  | Amihou     | *spondias cytherea* Senn. | roots          | 500               | 11.3          | 11.0          | 9.7           | 11        | 31 |
|    | Kwau       |            |                | 250               | 10.0          | 7.7           | 9.3           | 9         | 26 |
|    |            |            |                | 125               | 9.0           | 7.3           | 7.3           | 8         | 23 |
| 2  | Bikibeia   | *Ficus cf. anulata* Blume | leaves         | 500               | 12.0          | 10.7          | 11.0          | 11        | 33 |
|    | Kwau       |            |                | 250               | 9.3           | 9.7           | 10.0          | 10        | 28 |
|    |            |            |                | 125               | 7.3           | 8.0           | 8.3           | 8         | 23 |
| 3  | Bipasyom   | *Calophyllum peekeli* Luterb  | leaves         | 500               | 11.3          | 10.7          | 14.0          | 12        | 35 |
|    | Kwau       |            |                | 250               | 10.3          | 9.7           | 11.3          | 10        | 30 |
|    |            |            |                | 125               | 11.0          | 8.7           | 11.0          | 10        | 30 |
| 4  | Ciga       | *Pongamia Pinnata* (L.) Pierre | leaves         | 500               | 10.7          | 10.7          | 9.7           | 10        | 29 |
|    |            |            |                | 250               | 9.7           | 9.3           | 11.0          | 10        | 28 |
|    |            |            |                | 125               | 9.0           | 9.0           | 12.3          | 10        | 29 |
| 5  | Kopi       | *Coffee arabica* L. | leaves         | 500               | 31.3          | 30.7          | 30.7          | 31        | 100|
|    |            |            |                | 250               | 10.3          | 9.7           | 11.3          | 10        | 30 |
|    |            |            |                | 125               | 11.0          | 8.7           | 11.0          | 10        | 30 |
| 6  | Sirsak     | *Annona muricapa* L. | leaves         | 500               | 31.3          | 32.0          | 31.0          | 31        | 100|
|    |            |            |                | 250               | 0             | 0             | 0             | 0         | 0  |
|    |            |            |                | 125               | 0             | 0             | 0             | 0         | 0  |
| 7  | Musromah   | *Homolanthus sp.* | leaves         | 500               | 34.0          | 34.0          | 34.0          | 34        | 100|
|    |            |            |                | 250               | 7.3           | 9.7           | 10.3          | 9         | 27 |
|    |            |            |                | 125               | 7.3           | 7.0           | 8.3           | 8         | 22 |
| 8  | GInuia     | *Saurauia sp.* | leaves         | 500               | 32.3          | 33.3          | 33.7          | 33        | 100|
|    | Kwau       |            |                | 250               | 7.3           | 8.0           | 8.3           | 8         | 24 |
|    |            |            |                | 125               | 0             | 0             | 0             | 0         | 0  |
| 9  | Jetgora    | *Hydnopictum sp.* | leaves         | 500               | 33.3          | 34.7          | 33.0          | 34        | 100|
|    | Soub       |            |                | 250               | 0             | 0             | 0             | 0         | 0  |
|    |            |            |                | 125               | 0             | 0             | 0             | 0         | 0  |
| 10 | Tisia      | *Sida acuta* Burm.f. | barks          | 500               | 35.0          | 35.0          | 35.0          | 35        | 100|
|    | Kwau       |            |                | 250               | 12.7          | 9.7           | 10.7          | 11        | 31 |
|    |            |            |                | 125               | 10.0          | 8.3           | 9.3           | 9         | 26 |
| 11 | Kicar      | *Inocarpus fragiferua* Fokk. | barks          | 500               | 30.3          | 30.7          | 30.3          | 30        | 100|
|    |            |            |                | 250               | 8.7           | 9.0           | 9.3           | 9         | 30 |
|    |            |            |                | 125               | 9.3           | 9.0           | 8.7           | 9         | 30 |
| 12 | Komka      | *Pinelesodendron ambobinicum* (Hassk.) Miq. | barks          | 500               | 34.7          | 34.3          | 34.3          | 34        | 100|
|    | Mef        |            |                | 250               | 0             | 0             | 0             | 0         | 0  |
|    |            |            |                | 125               | 0             | 0             | 0             | 0         | 0  |
| 13 | Kama       | *Thibaudia sp.* | barks          | 500               | 35.0          | 35.0          | 35.0          | 35        | 100|
|    | Kwau       |            |                | 250               | 11.3          | 10.0          | 11.0          | 11        | 31 |
|    |            |            |                | 125               | 10.0          | 10.0          | 9.0           | 10        | 28 |
|    |            |            |                | 125               | 9.3           | 10.0          | 10.0          | 10        | 28 |

involves the membrane's breakdown by lipophilic components [17]. The mechanism of saponins' action as an anti-bacterial is to reduce surface tension resulting in increased permeability or leakage of cells, and resulting intracellular compounds will exit [16]. According to [18], this compound diffuses through the outer membrane and vulnerable cell walls, then binds to the cytoplasmic membrane and disrupts and reduces the
stability. This causes the cytoplasm to leak out of the cell, which results in cell death. Antimicrobial agents that interfere with the cytoplasmic membrane are bactericidal.

### 3.4. Anti-

Candida albican Fungi

Of the 13 types of plants researched in the Manokwari regency Kwau and Siau villages, there were ten Candida albican antifungal types. Three species are

**Table 5. Inhibitoryness of Medicinal Plants in Kwau and Siau Villages, Manokwari District as Anti Candida albican Fungi**

| No | Local Name     | Latin Name | Parts of used | Concent. (µg/well) | replication 1 | replication 2 | replication 3 | mean (mm) | % |
|----|----------------|------------|---------------|--------------------|---------------|---------------|---------------|------------|---|
| 1  | Amihou Kwau    | *spondias* | roots         | (+) 500 11 11 11 11 11 37 | 30 30 30 30 | 100 | | | |
|    |                | *clytherea*|               |                    | 250 10 10 10 10 10 34 | | | | | |
|    |                | Senn.      |               |                    | 125 9 9 9 9 9 31 | | | | | |
|    |                |            |               |                    | 250 9 9 9 9 9 29 | | | | | |
|    |                |            |               |                    | 125 7 7 7 7 7 25 | | | | | |
| 2  | Bikibeia Kwau  | *Ficus cf.* | leaves        | (+) 500 31 30 30 30 30 100 | 31 31 31 31 31 100 | | | | | |
|    |                | *anulata*  |               |                    | 250 18 18 18 18 18 58 | | | | | |
|    |                | Blume      |               |                    | 125 16 16 16 16 16 49 | | | | | |
| 3  | Bipasyomkwau   | *Calophyllum* | leaves       | (+) 500 31 30 30 30 30 100 | 31 31 31 31 31 100 | | | | | |
|    |                | *peekeli*  |               |                    | 250 17 17 17 17 17 54 | | | | | |
|    |                | Luterb     |               |                    | 125 15 15 15 15 15 49 | | | | | |
| 4  | Ciga           | *Pongamia* | leaves        | (+) 500 30 30 30 30 30 100 | 30 30 30 30 30 100 | | | | | |
|    |                | *Pinnata*  |               |                    | 250 9 9 9 9 9 30 | | | | | |
|    |                | (L.) Pierre|               |                    | 125 8 8 8 8 8 27 | | | | | |
| 5  | Kopi           | *Coffea*   | leaves        | (+) 500 30 30 30 30 30 100 | 30 30 30 30 30 100 | | | | | |
|    |                | arabica L. |               |                    | 250 9 9 9 9 9 30 | | | | | |
|    |                |            |               |                    | 125 8 8 8 8 8 27 | | | | | |
| 6  | Sirsak         | *Annona*   | leaves        | (+) 500 30 30 30 30 30 100 | 30 30 30 30 30 100 | | | | | |
|    |                | *municapa* |               |                    | 250 9 9 9 9 9 30 | | | | | |
|    |                | L           |               |                    | 125 8 8 8 8 8 27 | | | | | |
| 7  | Musromah Siau  | *Homolanthus* | leaves      | (+) 500 30 30 30 30 30 100 | 30 30 30 30 30 100 | | | | | |
|    | Siau           | sp.        |               |                    | 250 11 11 11 11 11 35 | | | | | |
|    |                |            |               |                    | 125 10 10 10 10 10 32 | | | | | |
| 8  | Ginuia Kwau    | *Saurauia* | leaves        | (+) 500 30 30 30 30 30 100 | 30 30 30 30 30 100 | | | | | |
|    |                | sp.        |               |                    | 250 9 9 9 9 9 30 | | | | | |
|    |                |            |               |                    | 125 8 8 8 8 8 27 | | | | | |
| 9  | Jetgora Soub/  | *Hydnopictum* | leaves      | (+) 500 31 31 31 31 31 100 | 31 31 31 31 31 100 | | | | | |
|    | Pohon Siau     | sp.        |               |                    | 250 10 10 10 10 10 32 | | | | | |
|    |                |            |               |                    | 125 9 9 9 9 9 30 | | | | | |
| 10 | Tisia Kwau     | *Sida*     | barks         | (+) 500 30 30 30 30 30 100 | 30 30 30 30 30 100 | | | | | |
|    |                | *acuta*    |               |                    | 250 11 11 11 11 11 35 | | | | | |
|    |                | Burm.f.    |               |                    | 125 9 9 9 9 9 30 | | | | | |
| 11 | Kikar          | *Inocarpus* | barks         | (+) 500 30 30 30 30 30 100 | 30 30 30 30 30 100 | | | | | |
|    |                | *fragiferus*|               |                    | 250 11 11 11 11 11 35 | | | | | |
|    |                | Fosk       |               |                    | 125 9 9 9 9 9 30 | | | | | |
| 12 | Komka Mef      | *Pimelodendron* | barks       | (+) 500 30 30 30 30 30 100 | 30 30 30 30 30 100 | | | | | |
|    |                | *amboinicum*|               |                    | 250 9 9 9 9 9 28 | | | | | |
|    |                | (Hassk.) Mq.|               |                    | 125 7 7 7 7 7 25 | | | | | |
| 13 | Kama Kwau      | *Thibaudia* | barks         | (+) 500 30 30 30 30 30 100 | 30 30 30 30 30 100 | | | | | |
|    |                | sp.        |               |                    | 250 9 9 9 9 9 28 | | | | | |
|    |                |            |               |                    | 125 7 7 7 7 7 25 | | | | | |

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plants that cannot inhibit the growth of *Candida albicans* mushrooms. Table 5. shows that medicinal plants in the Arfak range have different inhibitory effects on *Candida albicans* fungi. Secondary metabolite compounds in medicinal plants in the Kwau and Siau villages of Manokwari Regency are alkaloids, flavonoids, steroids, tannins, saponins, triterpenoids, carotenoids, and coumarin. The presence of secondary metabolites in various medicinal plants causes different inhibitory forces. Therefore the inhibitory power varies from weak to very strong. Secondary metabolites' content is thought to inhibit fungi' growth, especially the fungus *Candida albicans* [19]. Secondary metabolites in plants with moderate to strong inhibitory properties are flavonoids, tannins, saponins, and triterpenoids.

**Table 6. Inhibitory Power of Medicinal Plants in Kwau and Siau Villages, Manokwari Regency as Anti-Bacterial Escherichia coli**

| No | Local Name         | Latin Name                  | Parts of used | Concent. (µg/well) | Replication 1 | Replication 2 | Replication 3 | mean (mm) | %   |
|----|--------------------|-----------------------------|---------------|--------------------|---------------|---------------|---------------|-----------|-----|
| 1  | Amihou Kwau        | *Spondias cytherea* Senn.  | roots         | (+)                | 30            | 30            | 30            | 30        | 100 |
|    |                    |                             |               | 500                 | 11            | 11            | 11            | 11        | 37  |
|    |                    |                             |               | 250                 | 11            | 10            | 10            | 10        | 34  |
|    |                    |                             |               | 125                 | 10            | 9             | 10            | 10        | 32  |
| 2  | Bikibeia Kwau      | *Ficus cf. amalata* Blume  | leaves        | (+)                | 31            | 30            | 30            | 30        | 100 |
|    |                    |                             |               | 500                 | 10            | 9             | 9             | 9         | 31  |
|    |                    |                             |               | 250                 | 10            | 9             | 8             | 9         | 29  |
|    |                    |                             |               | 125                 | 8             | 7             | 7             | 8         | 25  |
| 3  | Bipasyomkwau       | *Calophyllum peekeli* Laterb| leaves        | (+)                | 31            | 31            | 31            | 31        | 100 |
|    |                    |                             |               | 500                 | 19            | 18            | 18            | 18        | 58  |
|    |                    |                             |               | 250                 | 17            | 17            | 16            | 17        | 54  |
|    |                    |                             |               | 125                 | 15            | 15            | 16            | 15        | 49  |
| 4  | Ciga               | *Pongamia Pinnata* (L.) Pierre| leaves    | (+)                | 30            | 30            | 30            | 30        | 100 |
|    |                    |                             |               | 500                 | -             | -             | -             | -         | -   |
|    |                    |                             |               | 250                 | -             | -             | -             | -         | -   |
|    |                    |                             |               | 125                 | -             | -             | -             | -         | -   |
| 5  | Kopi               | *Coffee arabica* L.         | leaves        | (+)                | 31            | 30            | 30            | 30        | 100 |
|    |                    |                             |               | 500                 | -             | -             | -             | -         | -   |
|    |                    |                             |               | 250                 | -             | -             | -             | -         | -   |
|    |                    |                             |               | 125                 | -             | -             | -             | -         | -   |
| 6  | Sirsak             | *Annona muricapa* L.       | leaves        | (+)                | 30            | 31            | 30            | 30        | 100 |
|    |                    |                             |               | 500                 | 9             | 10            | 10            | 10        | 32  |
|    |                    |                             |               | 250                 | 9             | 9             | 9             | 9         | 30  |
|    |                    |                             |               | 125                 | 8             | 8             | 8             | 8         | 27  |
| 7  | Musromah Siau      | *Homolanthus sp.*          | leaves        | (+)                | 30            | 30            | 30            | 30        | 100 |
|    |                    |                             |               | 500                 | 13            | 11            | 14            | 12        | 41  |
|    |                    |                             |               | 250                 | 10            | 11            | 10            | 10        | 35  |
|    |                    |                             |               | 125                 | 10            | 11            | 8             | 10        | 32  |
| 8  | Giniuia Kwau       | *Saurauia sp.*             | leaves        | (+)                | 30            | 30            | 30            | 30        | 100 |
|    |                    |                             |               | 500                 | -             | -             | -             | -         | -   |
|    |                    |                             |               | 250                 | -             | -             | -             | -         | -   |
|    |                    |                             |               | 125                 | -             | -             | -             | -         | -   |
| 9  | Jetgora Soub/ Pohon | *Hydnopictum sp*           | leaves        | (+)                | 31            | 31            | 31            | 31        | 100 |
|    |                    |                             |               | 500                 | 9             | 10            | 10            | 10        | 32  |
|    |                    |                             |               | 250                 | 10            | 9             | 10            | 10        | 32  |
|    |                    |                             |               | 125                 | 7             | 9             | 9             | 8         | 27  |
| 10 | Tisia Kwau         | *Sida acuta* Burm.f.       | barks         | (+)                | 31            | 31            | 31            | 31        | 100 |
|    |                    |                             |               | 500                 | 13            | 13            | 13            | 13        | 42  |
|    |                    |                             |               | 250                 | 11            | 11            | 11            | 11        | 35  |
|    |                    |                             |               | 125                 | 9             | 10            | 9             | 9         | 30  |
| 11 | Kikar              | *Inocarpus fragiferua* Fosk.| barks        | (+)                | 31            | 31            | 30            | 31        | 100 |
|    |                    |                             |               | 500                 | 12            | 13            | 13            | 12        | 40  |
|    |                    |                             |               | 250                 | 12            | 11            | 11            | 11        | 37  |
|    |                    |                             |               | 125                 | 11            | 9             | 10            | 10        | 33  |
| 12 | Komka Mef          | *Pinelodendron amboinicum* (Hassk.) Miq. | barks | (+) | 31 | 31 | 32 | 31 | 100 |
|    |                    |                             |               | 500                 | 11            | 10            | 11            | 10        | 33  |
|    |                    |                             |               | 250                 | 9             | 9             | 9             | 9         | 28  |
|    |                    |                             |               | 125                 | 8             | 7             | 7             | 8         | 25  |
| 13 | Kama Kwau          | *Thibaudia sp.*            | barks         | (+)                | 30            | 30            | 30            | 30        | 100 |
|    |                    |                             |               | 500                 | 11            | 11            | 11            | 11        | 36  |
|    |                    |                             |               | 250                 | 9             | 10            | 10            | 10        | 33  |
|    |                    |                             |               | 125                 | 9             | 9             | 7             | 8         | 28  |
3.5. Anti-Bacterial Escherichia coli

Of the 13 types of plants researched in the Manokwari regency Kwau and Siau villages, ten kinds of Escherichia coli anti-bacterial species and three species could not inhibit the growth of Escherichia coli bacteria. Table 6 shows that medicinal plants in the Arfak range have different inhibitory effects on Escherichia coli bacteria. Secondary metabolite compounds in medicinal plants in the Kwau and Siau villages of Manokwari Regency are alkaloids, flavonoids, steroids, tannins, saponins, triterpenoids, carotenoids, and coumarin. Of these 13 types, eight types contain flavonoids, and four types contain terpenoids. Flavonoid compounds can form complexes

| No | Local Name | Latin Name                              | Parts of used | Concent. (µg/well) | Replication 1 | Replication 2 | Replication 3 | mean (mm) | % |
|----|------------|-----------------------------------------|---------------|-------------------|---------------|---------------|---------------|-----------|----|
| 1  | Amihou Kwau | Spondias cytherea Senn.                 | roots         | (+)               | 31            | 32            | 32            | 32        | 100|
|    |            |                                         |               | 500              | -             | -             | -             | -         |    |
|    |            |                                         |               | 250              | -             | -             | -             | -         |    |
|    |            |                                         |               | 125              | -             | -             | -             | -         |    |
| 2  | Bikibeia Kwau | Ficus cf. anulata Blume                 | leaves        | (+)               | 31            | 31            | 31            | 31        | 100|
|    |            |                                         |               | 500              | -             | -             | -             | -         |    |
|    |            |                                         |               | 250              | -             | -             | -             | -         |    |
|    |            |                                         |               | 125              | -             | -             | -             | -         |    |
| 3  | Bipasyomkwau | Calophyllium peekeli Laterb             | leaves        | (+)               | 30            | 30            | 30            | 30        | 100|
|    |            |                                         |               | 500              | 15            | 15            | 15            | 15        | 50 |
|    |            |                                         |               | 250              | 12            | 12            | 13            | 13        | 41 |
|    |            |                                         |               | 125              | 11            | 10            | 11            | 11        | 35 |
| 4  | Ciga        | Pongamia pinnata (L.) Pierre            | leaves        | (+)               | 30            | 30            | 30            | 30        | 100|
|    |            |                                         |               | 500              | 10            | 13            | 11            | 11        | 38 |
|    |            |                                         |               | 250              | 9             | 9             | 10            | 9         | 31 |
|    |            |                                         |               | 125              | 8             | 9             | 9             | 9         | 29 |
| 5  | Kopi        | Coffea arabica L                        | leaves        | (+)               | 30            | 30            | 30            | 30        | 100|
|    |            |                                         |               | 500              | -             | -             | -             | -         |    |
|    |            |                                         |               | 250              | -             | -             | -             | -         |    |
|    |            |                                         |               | 125              | -             | -             | -             | -         |    |
| 6  | Sirsak      | Annona muricapa L                      | leaves        | (+)               | 30            | 30            | 30            | 30        | 100|
|    |            |                                         |               | 500              | 10            | 13            | 11            | 11        | 38 |
|    |            |                                         |               | 250              | 9             | 9             | 10            | 9         | 31 |
|    |            |                                         |               | 125              | 8             | 9             | 9             | 9         | 29 |
| 7  | Musromah    | Homalanthus sp.                        | leaves        | (+)               | 32            | 32            | 32            | 32        | 100|
|    | Siau        |                                         |               | 500              | -             | -             | -             | -         |    |
|    |            |                                         |               | 250              | -             | -             | -             | -         |    |
|    |            |                                         |               | 125              | -             | -             | -             | -         |    |
| 8  | Ginnua Kwau | Saurauia sp.                            | leaves        | (+)               | 30            | 30            | 30            | 30        | 100|
|    |            |                                         |               | 500              | -             | -             | -             | -         |    |
|    |            |                                         |               | 250              | -             | -             | -             | -         |    |
|    |            |                                         |               | 125              | -             | -             | -             | -         |    |
| 9  | Jêtgora Soub/ Pohon | Hydnopictum sp | leaves        | (+)               | 30            | 30            | 30            | 30        | 100|
|    |            |                                         |               | 500              | 9             | 9             | 10            | 9         | 31 |
|    |            |                                         |               | 250              | 9             | 9             | 8             | 9         | 29 |
|    |            |                                         |               | 125              | 8             | 9             | 7             | 8         | 27 |
| 10 | Tisia Kwau  | Sida acuta Burm.f.                     | barks         | (+)               | 32            | 32            | 32            | 32        | 100|
|    |            |                                         |               | 500              | -             | -             | -             | -         |    |
|    |            |                                         |               | 250              | -             | -             | -             | -         |    |
|    |            |                                         |               | 125              | -             | -             | -             | -         |    |
| 11 | Kikar       | Inocarpus fragiferus                    | barks         | (+)               | 31            | 31            | 31            | 31        | 100|
|    |            |                                         |               | 500              | -             | -             | -             | -         |    |
|    |            |                                         |               | 250              | -             | -             | -             | -         |    |
|    |            |                                         |               | 125              | -             | -             | -             | -         |    |
| 12 | Komka Mef   | Pimeledendron                           | barks         | (+)               | 30            | 30            | 30            | 30        | 100|
|    |            |                                         |               | 500              | -             | -             | -             | -         |    |
|    |            |                                         |               | 250              | -             | -             | -             | -         |    |
|    |            |                                         |               | 125              | -             | -             | -             | -         |    |
| 13 | Kama Kwau   | Thibaudia sp.                           | barks         | (+)               | 30            | 30            | 30            | 30        | 100|
|    |            |                                         |               | 500              | -             | -             | -             | -         |    |
|    |            |                                         |               | 250              | -             | -             | -             | -         |    |
|    |            |                                         |               | 125              | -             | -             | -             | -         |    |
with bacterial cell proteins through hydrogen bonds. The cell wall structure and cytoplasmic membrane of the bacteria containing the protein become unstable because the bacterial cells’ protein structure becomes damaged due to the hydrogen bond with flavonoids. The bacterial cell protein loses its biological activity.

As a result, bacterial cells’ permeability function is disrupted, and bacterial cells will undergo lysis, which results in bacterial cell death [20]. Inside, the flavonoids contain a phenol compound. *Staphylococcus aureus* bacterial growth can be disrupted due to phenol compounds. Phenol is acidic alcohol, so it is also called carboxlic acid. Phenol has the ability to denaturation proteins and damage cell membranes. Acidic conditions by the presence of phenol can affect the growth of *Staphylococcus aureus* bacteria [21]. The flavonoids in them can damage the bacterial cell wall so that the cell’s main components come out and cause bacterial cell death and inhibit cell protein formation. While tannins play a role in damaging cell membranes and alkaloids play a role in protein denaturation [22]. Akway extract (*Drimys piperita* Hook f.) Containing flavonoids and terpenoids is reported to inhibit verotoxigenic *Escherichia coli* in agar medium [23].

### 3.6. Anti-Bacterial *Streptococcus sobrinus*

Of the 13 types of plants researched in the Manokwari regency Kwau and Siau villages, there were ten types of *Streptococcus sobrinus* anti-bacterial species and three species not inhibit the growth of *Streptococcus sobrinus* bacteria. Table 7. shows that medicinal plants in the Arfak range have different inhibitory effects on *Escherichia coli* bacteria. Secondary metabolite compounds in medicinal plants in the Kwa and Siau villages of Manokwari Regency are alkaloids, flavonoids, steroids, tannins, saponins, triterpenoids, carotenoids, and coumarin. Secondary metabolites in various medicinal plants cause different inhibitory forces; therefore, the inhibitory power varies from moderate to strong [15].

#### 3.7. Toxicity

Brine Shrimp Lethality Test (BSLT) can be an initial selection of active compounds in plant extracts because it is relatively inexpensive fast and the results can be trusted and an initial screening of anti-cancer drugs. Toxicity test for shrimp larvae *Artemia salina* Leach using BSLT method can be used as a preliminary / pre-screening test to research compounds that lead to cytotoxic activity tests [21]. LC50 value of extract or compound was tested less than 1000 µg / mL (ppm), which is considered to indicate biological activity, so this test can be used as an initial screening of bioactive compounds which are thought to be productive as anticancer [24].

The results of the toxicity test of extracts of 13 types of medicinal plants can be seen in Table 9. From the table, there are two types of plants that have a toxicity effect on *Artemia salina* Leach, namely the root of *spondias cytherea* Senn. LC50 value of 91 ppm and leaves of *Inocarpus fragiferua* Fosk. LC50 value of 405 ppm. Root *spondias cytherea* Senn. and leaves of *Inocarpus fragiferua* Fosk. potential as a cancer drug. This was supported by the Mayer (1982) [25] study which stated that an extract showed ketoxic activity in Brine shrimp lethality test (BSLT) if the extract could cause 50% death of test animals at a concentration of LC50 <1000 ppm.

| No | Local Name   | Latin Name                  | Parts of used | Average death of Conc. | Average death of Conc. | percent of deaths LC50 |
|----|--------------|-----------------------------|---------------|------------------------|------------------------|------------------------|
| 1  | Amihou Kwau  | *Spondias cytherea* Senn.   | roots         | 10 10 0 100            | 100 0 0 0              | 91                     |
| 2  | Bikibeia Kwau| *Ficus cf. anulata* Blume   | leaves        | 0 0 0 0               | 0 0 0 0               | 0                      |
| 3  | Bipasyomkwau | *Calophyllum peckeli*       | leaves        | 0 0 0 0               | 0 0 0 0               | 0                      |
| 4  | Ciga         | *Pongamia Pinnata* (L.) Pierre | leaves       | 0 0 0 0               | 0 0 0 0               | 0                      |
| 5  | Kopi         | *Coffeea arabica* L.        | barks         | 0 0 0 0               | 0 0 0 0               | 0                      |
| 6  | Sirsak       | *Annona muricapa* L.       | leaves        | 0 0 0 0               | 0 0 0 0               | 0                      |
| 7  | Musromah     | *Homoluathus sp.*          | leaves        | 0 0 0 0               | 0 0 0 0               | 0                      |
| 8  | Ginuia Kwau  | *Sauria* sp.               | leaves        | 0 0 0 0               | 0 0 0 0               | 0                      |
| 9  | Jetgora Soub | *Hydnpictum sp*            | barks         | 0 0 0 0               | 0 0 0 0               | 0                      |
| 10 | Tisia Kwau   | *Sida acuta* Burm.f.       | leaves        | 0 0 0 0               | 0 0 0 0               | 0                      |
| 11 | Kikar        | *Inocarpus fragiferua* Fosk. | leaves       | 10 4 0 100            | 40 0 0 405            | 0                      |
| 12 | Komka Mef    | *Pimeleodendron* amboicinum (Hassk.) | leaves     | 0 0 0 0               | 0 0 0 0               | 0                      |
| 13 | Kama Kwau    | *Thibaudia* sp.            | leaves        | 0 0 0 0               | 0 0 0 0               | 0                      |
4. CONCLUSION

That methanol extract showed good activity against acne in only 8 of 13 species, ten types of 13 types for *E. coli*, three types of 13 types for *S. sobrinus* and, ten types of 13 types for *C. albicans* at 25-500 ppm of extract tested. The toxicity test showed that 0% of the deaths from *A. salina* Leach shrimp indicated that the absence of harmful compounds was toxic in the sample, meaning that it was very safe to be consumed directly by humans, except for the roots of *Spontias cytherea* Senn and the bark of *Inocarpus fragiferua* Fosk. Medicinal plants in the Siau and Kwau villages have strong antimicrobial and antioxidant properties to be used to develop medicinal plants in Indonesia.

REFERENCES

[1] F.T. Kapisa, Pemanfaatan Jenis Tumbuhan Obat oleh Masyarakat Suku Moor di Kampung Kama Pulau Moor Kabupaten Nabire, Skripsi Sarjana Kehutanan Universitas Negeri Papua, 2005.

[2] F.Y. Wulandari, Tanaman Obat Indonesia. Pusat Dokumentasi dan Informasi Manggala Wanabakti, Jakarta, 2001.

[3] I.W. Kusuma, H. Kuspradini, E.T. Arung, F. Aryani, Y-H. Min, J-S. Kim, Y-U. Kim, Biological Activity and Phytochemical Analysis of Three Indonesian Medicinal Plants, *Murraya koenigii*, *Syzygium polyanthum* and *Zingiber purpurea*, Journal of Acupuncture and Meridian Studies, 4(1), 2011, pp. 75-79.

[4] N.P. Jones, J.T. Arnason, M. Abou-Zaïd, K. Akpagana, P. Sanchez-Vindas, M.L. Smith, Antifungal Activity of Extracts From Medicinal Plant Used by First Nation Peoples of Eastern Canada, Journal of Ethnopharmacology, 73, 2000, pp. 191-198.

[5] N.S. Erma, T. Sundari, A.I. Susyanty, D.R.O. Palupi, Isnaeni, Sukardiman, Kajian Pendahuluan Uji Toksisitas Ekstrak Air Miselia dan Tubuh Buah Jamur Shiitake (*Lentinus edodes*) dengan Metode Brine Shrimp Lethality Test (BSLT), Berk. Penel. Hayati 10, 2004, 13-18.

[6] C.K. Kokate, Pharmacognosy 16th End, Niali Prakasham, Mumbai, India, 2001.

[7] J.B. Harborne, Metode Fitokimia, Penuntun cara modern menganalisis tumbuhan, (Terjemahan Kosasih Pamawinata dan Iwang Soediro), Penerbit ITB, Bandung, 1987.

[8] G. Senthilmurugan, B. Vasanthe, K. Suresh, Screening and Antibacterial Activity Analysis of some Important Medicinal Plants, International Journal of Innovation and Applied Studies, 2(2), 2013, pp. 146-152.

[9] H.R. Romadanan, D.L. Sitl, Shanti, Pengujian Aktivitas Antioksidan Ekstrak Bunga Lotus (*Nelumbo nucifera*), Fishtech, III(01), 2014.

[10] T.D. Wahyuni, B.W. Simon, Pengaruh Jenis Pelarut Dan Lama Ekstraksi Terhadap Ekstrak Karotenoid Labu Kuning Dengan Metode Gelombang Ultrasonik, Jurnal Pangan dan Agroindustri, 3(2), 2015, pp. 390-401.

[11] M. Sayuti, Pengaruh Perbedaan Metode Ekstraksi, Bagian dan Jenis Pelarut Terhadap Rendemen dan Aktifitas Antioksidan Bambu Laut (*Isis hippuris*), Technology Science and Engineering Journal, 1(3) 2017.

[12] S. Prawiroharsono, Benarkah tempe sebagai anti kanker, Jurnal Kedokteran dan Farmasi MEDIKA, 12(XXIV), 1998, pp. 815-817.

[13] I.W. Kusuma, Murdiyanto, E.T. Arung, Syafirzal, Y-u. Kim, Antimicrobial and antioxidant properties of medicinal plants used by the Bentian tribe from Indonesia, Food Science and Human Wellness, 3, 2014, pp. 191-196.

[14] E. Hanani, M. Abdul, S. Ryan, Identifikasi Senyawa Antioksidan dalam Spons *Calysspongia Sp* Dari Kepulauan Seribu, Majalah Ilmu Kefarmasian, 11(3), 2005, pp. 127-133.

[15] M.M. Cowan, Plant Products as Antimicrobial Agents, Clinical Microbiology Reviews, 12, 1999, pp. 564-582.

[16] M.C. Nuria, A. Faizatun, Sumantri, Uji Antibakteri Ekstrak Etanol Daun Jarak Pagar (*Jatropha cuircas*) terhadap Bakteri *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, dan *Salmonella typhi* ATCC 1408, Jurnal Ilmu – ilmu Pertanian, 5, 2009, pp. 26-37.

[17] V. Bobbarala, Antimicrobial Agents, Intech, Croatia, 2012.

[18] G. Cefarelli, B.D. Abrosca, A. Fiorentino, A. Izzo, C. Mastellone, S. Pacifica, V. Piscopo, Free-Radical Scavenging and Antioxidant Activities of Secondary Metabolites from Reddened *Annuurca Apple Fruits*, J.Agric.Food Chem, 54, 2006, pp. 803-809.

[19] Pulungan, S.S. Ahmad, Antifungal Activity of Ethanol Extract of Leaves Curcuma (*Curcuma longa LINN.*) against Fungus Candida albicans, Jurnal Biologi Lingkungan, Industri, Kesehatan (BioLink), 3(2), 2017.
[20] J.B. Harborne, Metode Fitokimia: Penuntun Cara Modern Menganalisa Tumbuhan. Edisi II, Institut Teknologi Bandung, Bandung, 2003.

[21] P.W. Rahayu, Aktivitas Antimikroba Bumbu Masakan Tradisional Hasil Olahan Industri Terhadap Bakteri Patogen dan Perusak, Buletin Teknologi dan Industri Pangan, 11(2), 2000, pp. 42-48.

[22] I. Hafizah, I.A. Nur, F. Muhammad, Uji Aktivitas Antibakteri Ekstrak Metanol Rumput Laut (Eucheuma sp) Pada Berbagai Tingkat Konsentrasi Terhadap Pertumbuhan Bakteri Escherichia coli dan Staphylococcus aureus, 2018. http://ojs.uho.ac.id/index.php/medula/article/view/194/135. Accessed October 21, 2018.

[23] G.N. Cepeda, Daya hambat akway (Drimys piperita Hook f.) terhadap pertumbuhan Escherichia coli, J. Agrotek 1(3), 2008, pp. 41-50.

[24] Nuraini, I. Asriani, N. Iin, Identifikasi dan Karakterisasi Senyawa Bioaktif Antikanker dari Ekstrak Etanol Kulit Batang Kayu Bitti (Vitex cofassus), 2014, Available in http://journal.uin-alauddin.ac.id/index.php/alkimia/article/view/1668/1617

[25] B.N. Mayer, N.R. Ferrigni, J.E. Putnam, L.B. Jacobsen, D.E. Nichols, J.L. McLaughlin, Brine shrimp: a convenient general bioassay for active plant constituents, Planta Medica, 1982.