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Antimicrobial and Antioxidant Medicinal Plants in Kwau Village and Silau Villlage, 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. albican* 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 Warmare 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,

Japan). DMSO (dimethyl sulfoxide), sulfuric acid, hydrochloric acid, acetic anhydride, potassium iodide, and peptone were purchased from Merck (Darmstadt, Germany). Ascorbic acid, 1-naphthol, and bismuth (III) nitrate were obtained from Sigma (St. Louis, MO, USA). Nutrient agar was obtained from Difco (Detroit, MI, USA). Other chemicals were of HPLC grade or the highest purity commercially available.

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 LC_{50}.

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 carotenoids, 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	bikibeia 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	*Homolanthus* sp.	Leaves	51.9213	2.1722	4.18
8	ginuia kwau	*Saurauia* sp.	bark	236.5198	13.6885	5.79
9	Jetgora 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	Bikibeia 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	*Homolanthus* sp.	leaves	+	+	-	-	-	-	+	-
8	Ginuia Kwau	*Saurauia* sp.	barks	+	-	-	-	+	-	-	-
9	Jetgora 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*, Pierre, *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 acnes* bacteria. A positive result if an inhibition zone is formed around the well. After incubating for 24 hours at 37^0C, 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

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				100	0.012	96.25	15
					50	0.013	95.95	
					25	0.030	90.88	
1	Amihou	*Spondias cytherea* Senn.	Leaves	14.77	100	0.204	21.99	156
					50	0.241	26.85	
					25	0.257	37.99	
2	Bikibeia	*Ficus cf. anulata* Blume	Barks	3.99	100	0.064	80.55	20
					50	0.066	80.04	
					25	0.093	71.63	
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 Siau	*Homolanthus* sp.	Leaves	4.18	100	0.033	52.79	9
					50	0.078	76.39	
					25	0.155	89.87	
8	Ginuia	*Saurauia* sp.	Barks	5.79	100	0.129	76.39	85
					50	0.136	52.79	
					25	0.176	60.69	
9	Jetgora Soub/ Pohon	*Hydnopictum* sp	Roots	17.41	100	0.324	1.52	80
					50	0.253	23.00	
					25	0.105	68.09	
10	Tisia	*Sida acuta* Burm.f.	Leaves	6.88	25	0.101	73.96	110
					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	*Pimelodendron 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	

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 anti-bacterial 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 anti-bacterial 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 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 Kwau	*spondias cytherea* Senn.	roots	(+)	34.7	34.0	35.0	35	100
				500	11.3	11.0	9.7	11	31
				250	10.0	7.7	9.3	9	26
				125	9.0	7.3	7.3	8	23
2	Bikibeia Kwau	*Ficus cf. anulata* Blume	leaves	(+)	34.0	34.7	33.7	34	100
				500	12.0	10.7	11.0	11	33
				250	9.3	9.7	10.0	10	28
				125	7.3	8.0	8.3	8	23
3	Bipasyom Kwau	*Calophyllum peekeli* Luterb	leaves	(+)	35.0	35.0	33.7	35	100
				500	11.3	10.7	14.0	12	35
				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	(+)	35.0	35.3	35.0	35	100
				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	*Coffea arabica* L	leaves	(+)	31.3	30.7	30.7	31	100
				500	0	0	0	0	0
				250	0	0	0	0	0
				125	0	0	0	0	0
6	Sirsak	*Annona muricapa* L	leaves	(+)	31.3	32.0	31.0	31	100
				500	0	0	0	0	0
				250	0	0	0	0	0
				125	0	0	0	0	0
7	Musromah	*Homolanthus* sp.	leaves	(+)	34.0	34.0	34.0	34	100
				500	7.3	9.7	10.3	9	27
				250	7.3	7.0	8.3	8	22
				125	0	0	0	0	0
8	Ginuia Kwau	*Saurauia* sp.	leaves	(+)	32.3	33.3	33.7	33	100
				500	7.7	8.0	8.3	8	24
				250	0	0	0	0	0
				125	0	0	0	0	0
9	Jetgora Soub	*Hydnopictum* sp.	leaves	(+)	33.7	34.7	33.0	34	100
				500	0	0	0	0	0
				250	0	0	0	0	0
				125	0	0	0	0	0
10	Tisia Kwau	*Sida acuta* Burm.f.	barks	(+)	35.0	35.0	35.0	35	100
				500	12.7	9.7	10.7	11	31
				250	10.0	8.3	9.3	9	26
				125	9.0	7.7	7.3	8	23
11	Kikar	*Inocarpus fragiferua* Fosk	barks	(+)	30.3	30.7	30.3	30	100
				500	8.7	9.0	9.3	9	30
				250	9.3	9.0	8.7	9	30
				125	7.7	9.0	9.0	9	28
12	Komka Mef	*Pimelodendron amboinicum* (Hassk.) Miq.	barks	(+)	34.7	34.3	34.3	34	100
				500	9.0	10.7	11.0	10	30
				250	0	0	0	0	0
				125	0	0	0	0	0
13	Kama Kwau	*Thibaudia* sp.	barks	(+)	35.0	35.0	35.0	35	100
				500	11.3	10.0	11.0	11	31
				250	10.0	10.0	9.0	10	28
				125	9.3	10.0	10.0	10	28

involve 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. Inhibitiveness 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 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. anulata* 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* Luterb	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	*Coffea 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	Ginuia 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	*Pimelodendron 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

plants that cannot inhibit the growth of *Candida albican* mushrooms. Table 5. shows that medicinal plants in the Arfak range have different inhibitory effects on *Candida albican* 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. anulata* 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* Luterb	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	*Coffea 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	Ginuia 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	*Pimelodendron 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

Table 7. Inhibiting Power of Medicinal Plants in Kwau and Siau Villages, Manokwari Regency as Anti-Bacterial *Streptococcus sobrinus*

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	*Calophyllum peekeli* Luterb	leaves	(+)	30	31	30	30	100
				500	15	15	15	15	50
				250	13	12	13	13	41
				125	11	10	11	11	35
4	Ciga	*Pongamia pinnata* (L.) Pierre	leaves	(+)	31	31	33	32	100
				500	-	-	-	-	-
				250	-	-	-	-	-
				125	-	-	-	-	-
5	Kopi	*Coffea arabica* L	leaves	(+)	31	31	31	31	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 Siau	*Homolanthus* sp.	leaves	(+)	32	32	31	32	100
				500	-	-	-	-	-
				250	-	-	-	-	-
				125	-	-	-	-	-
8	Ginuia Kwau	*Saurauia* sp.	leaves	(+)	30	30	30	30	100
				500	-	-	-	-	-
				250	-	-	-	-	-
				125	-	-	-	-	-
9	Jetgora 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	33	32	100
				500	-	-	-	-	-
				250	-	-	-	-	-
				125	-	-	-	-	-
11	Kikar	*Inocarpus fragiferua* Fosk	barks	(+)	31	31	31	31	100
				500	-	-	-	-	-
				250	-	-	-	-	-
				125	-	-	-	-	-
12	Komka Mef	Pimelodendron amboinicum (Hassk.) Miq.	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 carbolic 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 Kwau 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 anti-cancer [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.

Table 8. Toxicity of medicinal plants in Kwau and Siau Villages, Manokwari Regency

No	Local Name	Latin Name	Parts of used	Average death			percent of deaths			LC50
				Conc. 1000 ppm	Conc. 100 ppm	Conc. 10 ppm	Conc. 1000 ppm	Conc. 100 ppm	Conc. 10 ppm	
1	Amihou Kwau	*Spondias cytherea* Senn.	roots	10	10	0	100	100	0	91
2	Bikibeia Kwau	*Ficus cf. anulata* Blume	leaves	0	0	0	0	0	0	0
3	Bipasyomkwau	*Calophyllum peekeli* Luterb	leaves	0	0	0	0	0	0	0
4	Ciga	*Pongamia Pinnata* (L.) Pierre	leaves	0	0	0	0	0	0	0
5	Kopi	*Coffea arabica* L	barks	0	0	0	0	0	0	0
6	Sirsak	*Annona muricapa* L	leaves	0	0	0	0	0	0	0
7	Musromah	*Homolanthus* sp.	leaves	0	0	0	0	0	0	0
8	Ginuia Kwau	*Saurauia* sp.	leaves	0	0	0	0	0	0	0
9	Jetgora Soub	*Hydnopictum* sp	barks	0	0	0	0	0	0	0
10	Tisia Kwau	*Sida acuta* Burm.f.	leaves	0	0	0	0	0	0	0
11	Kikar	*Inocarpus fragiferua* Fosk	leaves	10	4	0	100	40	0	405
12	Komka Mef	*Pimelodendron amboinicum* (Hassk.) Miq.	leaves	0	0	0	0	0	0	0
13	Kama Kwau	*Thibaudia* sp.	leaves	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.colii*, three types of 13 types for *S.sobrinus* and, ten types of 13 types for *C. albican* 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 *Spondias 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.

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