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Avicennia Marina: A Natural Resource for Male Anti-Fertility in Family Planning

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ABSTRACT

Increasing male involvement in family planning is a strategic priority, with herbal anti-fertility agents offering a potential solution. Coastal communities have traditionally utilized the bark of *Avicennia marina* as an anti-fertility agent. This study aims to characterize the bioactive compounds present in *A. marina* tissues and assess their potential as male anti-fertility agents. This exploration of mangrove anti-fertility agents could address the issue of limited access to contraceptives among low-income individuals residing in coastal regions. *A. marina* samples were collected from the mangrove forests of Pasir Sakti Village, Lampung Timur Regency. The bioactive content was analyzed using Gas Chromatography (Agilent 6890 series GC -MS) equipped with an HP-5MS method. A total of 49 bioactive compounds were identified in *A. marina* using the GC-MS method and ethanol solvent for extraction. The highest diversity of bioactive compounds was observed in flowers and fruits, followed by wood, roots, leaves, and bark, containing 21, 14, 13, 13, and 8 compounds, respectively. *A. marina* demonstrated the potential to produce 36 types of flavonoids, compounds previously established as effective male anti-fertility agents. The majority of flavonoids were found in the root, followed by flowers and fruits, wood, leaves, and bark, with 14, 11, 11, 8, and 8 types, respectively. These findings suggest that *A. marina* possesses significant potential as a source of male anti-fertility agents, presenting an opportunity to increase men's participation in family planning, especially in low-income coastal communities.

1. INTRODUCTION

The United Nations Department of Economic and Social Affairs (UN DESA) [1] forecasts a continued growth in world population, with a projected peak of 11 billion by 2100. This population surge is anticipated to be primarily concentrated in low and lower-middle-income countries, leading to demographic challenges and obstructing their escalation to high-income status [2]. Such rampant population growth presents a global challenge, raising concerns about ensuring sustainable, equitable, and inclusive future development [1].

Indonesia, a developing nation with the world's fourth-largest population, follows China, India, and the USA [1]. The Indonesian Central Bureau of Statistics (BPS) [3] states that the population stands at 275.77 million, with a yearly growth rate of 1.17% and a Total Fertility Rate of 2.42 per female. This considerable population growth is expected to spur an increased demand for natural resources that may result in environmental degradation [4]. Consequently, it is imperative for the government to take serious measures to control population growth as a reduced fertility rate aligns with improved welfare and health, reduced mortality, and increased education and urbanization [5]. Increased access to reproductive health services, including safe and effective family planning methods, is posited to help lower fertility and expedite economic and social development [1].

In response to the rising population, the Indonesian government has been implementing a family planning (KB) program since 1970. However, even after more than 50 years, gender equality remains a significant issue, with the participation rate for women reaching 97.30% and a meager 2.70% for men [6]. The development of male contraceptive agents has been slow and limited. The choices available for male contraception—condoms and vasectomy—are inadequate [6]. Condoms are not widely accepted due to their impact on the quality of sexual intercourse [7], and vasectomies are perceived as reducing men's sexual and physical capabilities [8]. Moreover, the potential side effects of hormonal contraception raise concerns among men [9, 10]. Anti-fertility agents serve as fertility control and are viewed as a primary solution to manage the population growth rate, particularly in developing countries [11]. Herbal contraception emerges as a promising alternative to male contraception, making its development strategic in increasing men's participation in family planning [12, 13].

Unlike women, who produce one egg per month, men generate millions of sperm cells daily, presenting a challenge to control male fertility. A compound is required that can regulate sperm production without diminishing libido or causing harmful side effects [2]. One potential avenue is the use of plant-based natural ingredients. Herbal medicines offer several advantages, including relatively fewer side effects, ease of access, affordability, and cultural acceptance [14, 15].

Indonesia, a mega-biodiverse nation, boasts approximately

30,000 plant species, with 7,000 indicated to possess medicinal properties [16]. This potential provides an excellent opportunity for Indonesia to produce male herbal anti-fertility, supporting scientific data from traditional medicine as a modality for preventing and treating various medical problems. Mangroves, a group of plants rich in bioactive compounds, grow and adapt in stressful and extreme environments, producing various secondary metabolic substances to cope with environmental stress [17].

Avicennia marina (*A. marina*), a prevalent mangrove species along the Indonesian coast, is known for its extraordinary adaptability, flexible growth pattern, and resistance to extreme weather and strong winds [18, 19]. Dense and extensive roots make *A. marina* an effective mud trapper and habitat for various marine biota [18]. In addition to its ecological role, *A. marina* is known to contain various secondary metabolic compounds like steroids, naphthalene, terpenoids, flavonoids, phenyl propanoid glycosides, diterpenoid glucosides, and glucoside iridoids [20, 21]. These compounds exhibit antimicrobial, antioxidant, antiaging, anti-inflammatory, antitumor, kidney anti-choline, anti-tuberculosis, and anti-atherosclerotic properties [22]. Flavonoids, in particular, have anti-fertility properties. Previous studies have shown that the flavonoid content in black tea exhibits anti-fertility properties in male rats [23]. Flavonoids, alkaloids, steroids, terpenoids, tannins, and saponins found in durian rind extract also exhibit activity as male anti-fertility [24]. Therefore, identifying the types of flavonoids in each *A. marina* tissue is crucial. The presence of flavonoids in *A. marina* would confirm its potential as an anti-fertility agent. The evidence of flavonoid compounds, especially in the bark of *A. marina*, provides scientific support for its use as an anti-fertility agent, a practice empirically conducted by Indonesian coastal communities for decades.

Lolok et al. [22] reported that *A. marina* stem bark extract was shown to have potential activity as an anti-fertility agent in male rats, as evidenced by a decrease in the number of spermatozoa, epididymal weight, viability, and motility. However, until now, there has been no report on the bioactive contained in *A. marina*, which acts as an anti-fertility agent, and in which tissues these compounds can be found. Furthermore, bark extraction is usually done by cutting or peeling a portion of the bark of a living tree. Both methods can potentially cause vegetation damage, create wounds that become entry points for pathogenic germs, and even cause plant death. Therefore, studying the content of anti-fertility compounds in *A. marina* on all kinds of plant tissues, especially those that can be harvested without threatening plant survival, is essential.

This study aims to explore the potential of *Avicennia marina* (*A. marina*) as a natural, herbal anti-fertility agent for males. Specifically, it seeks to identify the presence and types of flavonoids in various tissues of *A. marina*, including the bark, leaves, and roots. The results of this research can provide a scientific basis for the development of a novel, plant-based male contraceptive, contributing to the efforts to control the population growth in developing countries like Indonesia.

2. MATERIALS AND METHOD

2.1 Sampling

Samples of *A. marina* were taken from mangrove forests in Pasir Sakti Village, East Lampung Regency, the largest mangrove forest in Lampung, with an ecosystem facing the Java Sea. As much as 2 kg of fresh and healthy mangrove plant tissues (roots, stems, bark, flowers and fruits, and leaves) were taken from the field and cleaned of impurities by washing with distilled water. The samples of mangrove plant tissue were oven-dried at 80℃ until the weight was constant. Precisely, the tissue was chopped for mangrove root, stem, and bark tissue to produce flakes measuring less than 1 cm^3 to speed up the drying process. The oven-dried samples then powdered. Each (50 g) sample powder was macerated in 500 mL of 98% methanol for 12 hours and then filtered using filter paper. The solvent was evaporated using an evaporator to obtain liquid crude extract. The liquid crude extract was then analyzed using the GC-MS method. Maceration was chosen because it is simple and does not require complicated equipment. Methanol was used in this study because various compounds with different polarities (non-polar to polar) from plant samples can be extracted using this solvent.

2.2 GC-MS analysis

Analysis of the bioactive content in the liquid extract of each part of the mangrove plant was carried out by Gas Chromatography (Agilent 6890 series GC-MS) equipped with an HP-5MS column (diameter length 30 m; diameter 0.25 mm; film thickness 0.25 mm) mass spectrometer programmed at a temperature of 30℃ - 280/300℃ with a holding time of 5 minutes at a speed of 10℃/minute. Chromatographic conditions were a 1.2 ml/min column flow rate, injection mode: split, and carrier gas was Helium 99.999%. The mass spectral fragmentation pattern was compared to a spectrometer database using the National Institute of Standards and Technology Mass Spectral (NIST-MS) database. The percentage of each component is calculated from the relative peak area of each element in the chromatogram [25]. GC-MS is used because it is sensitive, efficient, and can separate complex mixtures of plant metabolites.

3. RESULT AND DISCUSSION

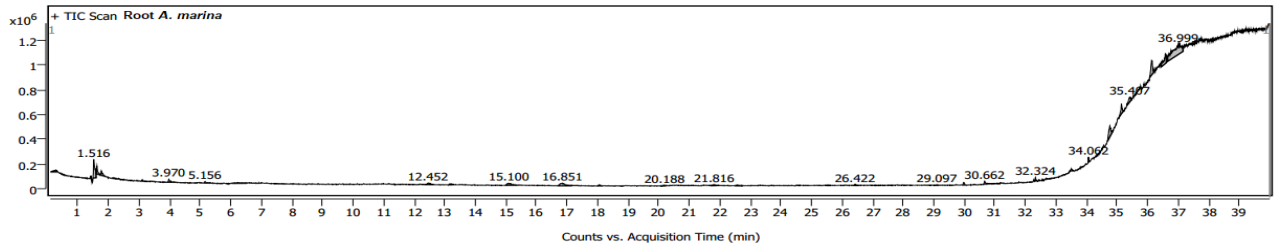
3.1 Bioactive compounds

The potential of mangrove plants as a source of herbal medicine has received little attention from the general public, academics, and the business world. Even though as a halophyte group, mangrove plants are unique because they can grow and adapt to specific habitats [26]. *A. marina* is a mangrove species adaptable to various habitat conditions. It can grow in freshwater swamps, muddy shores, mangrove areas, and substrates with very high salt content [18]. As a plant living in extreme environments, *A. marina* produces various secondary metabolic substances to cope with environmental stress and sustain life [17]. Secondary metabolic substances produced by mangrove plants have the potential to be used as bioactive that are beneficial to health.

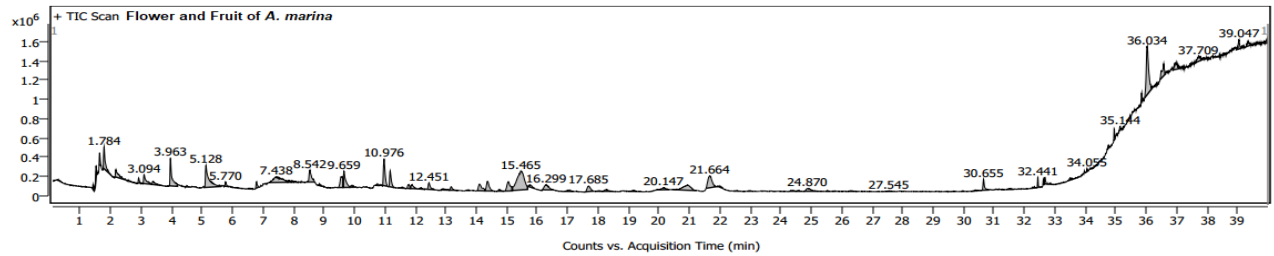
The result shows that at least 49 bioactive compounds identified in various tissues of *A marina* were extracted using the GC-MS method and ethanol solvent (Figure 1 and Table 1). The diverse bioactive compound of *A. marina* indicates that the plant has many medicinal benefits. In line with the report [27], the bioactive components of *A. marina* leaves are flavonoids, steroids, and reducing sugars. Regarding the bioactive content, *A. Marina* has been empirically used by the community as an antiulcer treatment for rheumatism, smallpox, and skin diseases [19, 28].

Nowadays, the biochemistry of plants has been widely studied [29, 30]. Gas Chromatography-Mass Spectrometry (GC-MS) is a reliable method of detecting bioactive components. The results showed that *A. marina* has many potential bioactive compounds for various therapeutic uses. The GC chromatogram shows the relative concentrations of the various eluted compounds as a function of retention time. Peak height indicates the relative concentration of the components presented. The mass spectrometer analyzes the compounds eluted at different times to identify the properties and structures of the compounds. This mass spectrum is a molded figure of the compound which can be identified from the database. The combination of GC and MS, the best separation and identification techniques, makes GC-MS an ideal method for qualitatively analyzing volatile and semivolatile bioactive compounds, especially in *A. marina*.

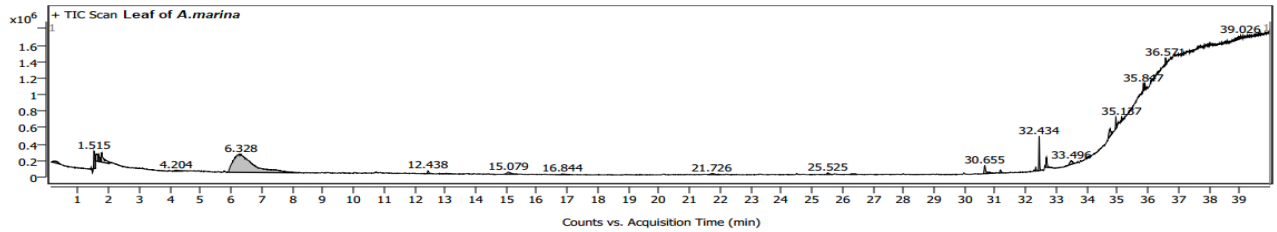
The plant bioactive content of *A. marina* was found in all plant tissues analyzed. Several bioactive compounds are found in all plant tissues, such as 10-Azido-1-decanethiol and Nona-2,3-dieonic acid, ethyl ester, but most of the bioactive compounds are found in each plant tissue are unique and not found in other plant tissues. It indicates that *A. marina* has enormous potential as a herbal medicine, and the efficacy of this plant is different for each type of plant tissue used. Each part of the plant has various abilities in accumulating secondary metabolic substances. The ability is interesting to study because each part of the plant can act as a factory that produces and provides substantial pharmaceutical potential.



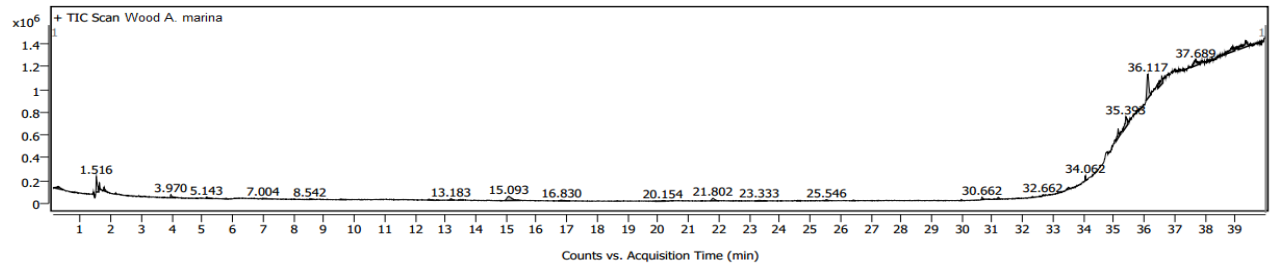
(a) Chromatograms of *A. marina* root extract



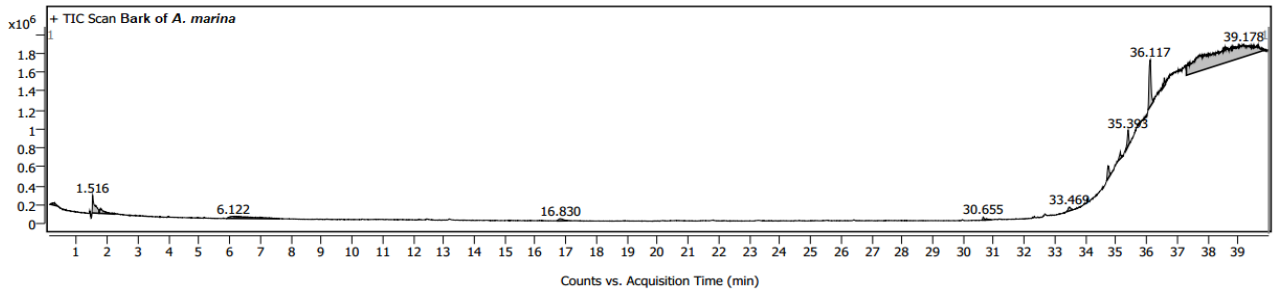
(b) Chromatograms of *A. marina* flower and fruit extract



(c) Chromatograms of *A. marina* leaf extract



(d) Chromatograms of *A. marina* wood extract



(e) Chromatograms of *A. marina* bark extract

Figure 1. Chromatograms of *A. marina* tissues extract

Table 1. Bioactive compounds of *A. marina*

No.	Compound	Molecular Formula	MW. g/mol	RT. (min)	Tissue				
					R	F	L	W	B
1	Bacteriochlorophyll-cstearyl	$C_{52}H_{72}MgN_4O_4$	841.50	36,999	+				
2	Betaine	$C_5H_{11}NO_2$	117.15	7,438		+			
3	Borane, compd. With dimethylamine 1:1	$C_2H_{10}BN$	58.92	6,328			+		
4	Borinic acid, diethyl-,1-cyclododecen-1-yl-ester	$C_{16}H_{31}BO$	250.20	39,047		+			
5	Borinyc acid, diethyl-	$C_4H_{11}BO$	85.94	15,169		+			
6	Cyclohexane,1-butenylidene-	$C_{10}H_{16}$	136.23	14,106		+			
7	Cyclododecyl isothiocyanate	$C_{13}H_{23}NS$	225.4	32,441		+			
8	Cyclopropaneoctanoic acid, 2-hexyl-, methyl ester	$C_{18}H_{34}O_2$	282.5	32,324	+				
9	Cis-1-Chloro-9-octadence	$C_{18}H_{35}Cl$	286.9	34,062	+	+		+	
10	Cyclohexaneamine, N-(2,3,4-trimethylhex-3--enylidine)-N-OXIDE	$C_{15}H_{27}NO$	237.38	36,124		+			
11	Cyclopropaneotctanic acid, 2-[[2-[(2-ethylcyclopropy]methyl]-,methyl ester]	$C_{22}H_{38}O_2$	334.50	37,079		+			
12	Docedanal	$C_{12}H_{24}O$	184.32	23,333				+	
13	Decanal	$C_{10}H_{20}O$	156.26	20,154				+	
14	Diazene, bis(3-methylcyclohexyl)-,1,2-dioxide	$C_{14}H_{26}N_2O_2$	254.37	13,500	+			+	+
15	E-7-Dodecen-1-ol-acetate	$C_{14}H_{26}O_2$	226.35	26,422	+				
16	Ethatone, 1-[5-(1,1dimethylethyl)-2-ethyl-4-methyl-1,3,2-dioxaborolan-4-yl]-	$C_{11}H_{21}BO_3$	212.10	21,082				+	
17	Hexadecaonic acid, 1-[[[(2-aminoethoxy) hydroxyphosphiny]oxy]methyl]-1,2-ethanediyl ester	$C_{37}H_{74}NO_8P$	692,00	35,407	+				
18	Lactic acid, monoanhydre wit h 1-butaneboronic acid, cyclic ester	$C_7H_{13}BO_3$	55.99	21,664		+			
19	Nona-2,3-dieonic acid, ethyl ester	$C_{11}H_{18}O_2$	182.26	1,419	+	+	+	+	+
20	n-Hexadecaonic acid	$C_{16}H_{32}O_2$	256.42	30,655		+	+		
21	n-Nonadecanol	$C_{19}H_{40}O$	284.50	35,847			+		
22	Oxacycloheptadecan-2-one	$C_{16}H_{30}O_2$	254.41	37,689				+	
23	Phytol	$C_{20}H_{40}O$	296.50	32,434			+		
24	Propylamine, N, N,2,2-Tetramethyl-, N-oxide	$C_7H_{17}NO$	131.22	3,963		+			
25	Pyridine,2-chloro-3-fluoro-,1-oxide	$C_5H_3C_lFNO$	147.53	15,079			+		
26	Ricinoleic acid	$C_{18}H_{34}O_3$	298.50	39,026			+		
27	Xylopyrasonide, methyl 4-azido-4-doxy-,beta-L-	$C_6H_{11}N_3O_4$	189.17	9,597		+			
28	z,z-2,15-Octadecdien-1-ol acetate	$C_{20}H_{36}O_2$	308.50	36,572			+		
29	1-Tridecyne	$C_{13}H_{24}$	180.33	21,816	+				
30	1-Nitrosikloheksena atau 2,5-Bis(hidroksimetil)pirol)	$C_6H_9NO_2$	127.14	3,094		+			
31	1,3-Propanediamine, N- (ethylcarbonimidoyl)-n,n-dimethyl	$C_8H_{17}N_3$	155.24	1,619			+		
32	1,3,2-Oxazabarobolane-4-carboxylic acid, 2-butyl-, methyl ester, L-	$C_8H_{16}BNO_3$	185.03	10,976		+			
33	(1(10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo[5,2,1,0(1,5)] dec-4-3-yl)-3-methylpent-4-en-1-one)	$C_{16}H_{25}NO_3S$	311.40	33,510	+		+	+	+
34	13-Octadecenal, (Z)	$C_{18}H_{34}O$	266.50	32,324					+
35	1,2 Oxathiane,6-dodecyl-,2,2-dioxide	$C_{16}H_{32}O_3S$	304.50	39,971					+
36	17-octadecynoic acid	$C_{18}H_{32}O_2$	280.40	36,117					+
37	(2-(2-(4-methyl-frurazan-3-yloxy)-ethyl)-2H-tetrazol-5-ylamine)	$C_6H_9N_7O_2$	211.18	8,542		+			
38	3-Azabutyl-1-ol, O-acetyl-4-cyclopropyl-N,N-dimethyl-, bromide	$C_{10}H_{20}NO_2$	186.27	4,494		+			
39	3-Diazo-1,7,7-trimethylbicyclo[2,2,1] heptan-2-one	$C_{10}H_{14}N_2O$	178.23	12,438			+		
40	3-Azonia-5-hexene-1-ol-,N,N-dimethyl-,carbamate ester, bromide;	$C_8H_{17}N_2O_2$	173.23	1,784		+			+
41	(3-Methyl-4-(phenythio)-2-prop-2-enyl-2,5-dihydrothiophene 1,1-dioxide)	$C_{14}H_{16}O_2S_2$	280.40	1,612	+				
42	4-Methyl-2,3-hexadien-1-ol	$C_7H_{12}O$	112.17	5,143		+		+	
43	4-Isopropyl-1,2,3-triazol-1-1-yl)acetic acid	$C_7H_{11}N_3O_2$	169.18	8,542				+	
44	4,5-Heptadien-2-one, 3,3,6-trimethyl	$C_{10}H_{16}O$	152.23	25,525			+	+	
45	8-Hexadecanal, 14-methyl-, (Z)	$C_{17}H_{32}O$	252.40	30,400	+			+	
46	10-Azido-1-decanethiol	$C_{10}H_{21}N_3S$	215.36	10,755	+	+	+	+	+
47	10-Methylundec-2-en-4-olide	$C_{12}H_{20}O_2$	196.29	24,870		+			
48	10-Methylcyclo[4,3,1,1(2,5)]undercan-10-ol	$C_{12}H_{20}O$	180.29	20,188	+				
49	17-Octadecyinic acid	$C_{18}H_{32}O_2$	280.40	36,117				+	
	Total				13	21	13	14	8

MW is molecular weight, RT is retention time, R is root, FF is fruit and flower, L is leaf, W is wood, and B is bark.

Table 1 shows 22 bioactive compounds in the flowers and fruits of *A. marina*. The result aligns with the report [31] that *A. Marina* is rich in bioactive compounds, namely the aliphatic group alcohols and acids, hydrocarbons, amino acids, alkaloids, free fatty acids, carbohydrates, carotenoids, pheromone, phorbolesters, phenolics and related compounds, lipids, triterpenes, steroids, and their glycosides, tannins, and other terpenes. In general, flowers and fruit have a higher

nutritional content than other plant tissues. A fruit is a plant's reproductive structure, designed to provide nutrition for the seeds that develop within it. Therefore, fruits are often high in vitamins, minerals, and antioxidants. It indicates that using fruit as part of the plant for treatment has tremendous potential compared to other tissues. The nature of *A. marina* supports it as a flowering and fruiting plant throughout the year. *A. marina* fruit is also categorized as edible, has a good taste, and can be made into various processed foods. There are at least nine mangrove species that produce edible fruit and have been widely consumed by people in Indonesia, namely *A. marina*, *A. alba*, *Bruguiera gymnorrhiza*, *Sonneratia alba*, *S. cassiolaris*, *Nypa fruticans*, *Rhizophora mucronata*, *R. apiculata* and *R. Stylosa* [32, 33].

The results showed that the bioactive compounds in *A. marina* leaves were not as abundant as those in flowers and fruits, such as wood. However, the potential of the leaf as a source of herbal medicine is high because it has a variety of specific bioactive compounds not found in other plant tissue parts. *A. marina* leaves contain alkaloids, terpenoids, and flavonoids and are antibacterial against Staphylococcus aureus bacteria [34]. *A. marina* leaf extract is effective as an antiviral, antinematode, antimalarial, and cytotoxic [35, 36]. Miles et al. [37] reported that *A. marina* leaves have long been used in traditional medicine to treat skin diseases, rheumatism, smallpox, boils, and animal feed on farms.

The leaves are dominantly used as medicinal ingredients because of their ease of harvesting, capability to grow back, and availability throughout the year [38, 39]. The people's preference for utilizing leaves as a source of herbal medicine is also related to the ease of extracting the phytochemical content compared to other parts. Mulyani et al. [40] stated that handling and extracting the phytochemical content from the leaves is easier. In addition to reasons of availability and ease of harvesting and extraction, the high utilization of leaves is also related to the survival rate of the plants. Leaf harvesting has little potential to cause damage and plant death.

Extraction of leaf biomass within reasonable limits tends not to disturb plant life much, compared to other parts (stems, roots, or bark) that can endanger plant life. *A. marina* bark has been trusted by many people in various parts of the world as an anti-fertility herb. However, it turns out that the bark of *A. marina* has several types of bioactive compounds that are not as high as other tissues. Several bioactive compounds in the stem bark are also found in other parts. If not done carefully, harvesting the bark can disrupt the tree's survival. However, the stem bark of *A. marina* also has specific compounds that are not found in other tissues, so its potential as a herbal medicine needs to be studied further.

A. marina has massive, widespread roots with pneumatophore breath roots [41]. The content of bioactive compounds found in the roots of *A. marina* is also quite diverse, although not as much as in the flowers and fruit, as well as wood. Using roots as herbal medicinal is also very promising because this part is easy to harvest, does not potentially harm plant life, and contains various and specific bioactive compounds not found in other tissues.

A.marina wood contains diverse bioactive compounds and is the second most varied after flowers and fruit. It indicates that the potential of *A. marina* wood tissue as a herbal medicine is very high. However, timber harvesting can threaten plant life, so it must be used wisely. In addition to the various types, the content of bioactive compounds in *A. marina* wood is also classified as specific and is not found in other tissues. Therefore the potential of each bioactive compound contained in *A. marina* wood tissue is significant to study to find new drug sources.

The results showed several components of bioactive compounds found in five mangrove plant tissues: Nona-2,3-dienoic acid, ethyl ester, and 10-Azido-1-decanethiol. Compound (1(10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo [5,2,1,0 (1,5)]dec-4-3-yl)-3-methyl pent- 4-en-1-one) is a compound found in all plant tissues except in flowers and fruit. Diazene, bis(3-methyl cyclohexyl)-,1,2-dioxide is found in bark, root, and wood tissues. Cis-1 compounds -Chloro-9-cadence was found in stem bark, roots, and wood. Compound 8-Hexadecanal, 14-methyl-, (Z) was found in root and wood. It indicates that if the bioactive is present in two or more plant tissues, then the extraction of these compounds for medicinal purposes should be carried out on the tissues that are easiest to be harvested and do not have the potential to harm plant life. In line with the opinion of Nisyapuri [29], leaves are the most easily utilized part of a plant species; leaves also contain many medicinal properties. Harvesting stems in large quantities will also cause damage to mangrove plants [42].

The bioactive content of plants can be helpful as an anti-fertility agent, both for men and women. In males, bioactive compounds can produce sperm abnormalities due to cessation of spermatogenesis, degeneration in the seminiferous tubules, and regression of Leydig cells were also observed [43]. In addition, plant extracts can cause teratogenic effects due to their oxidative activity, which can cause DNA fragmentation in somatic cells [44, 45]. Flavonoids are one of the bioactive groups that have been widely proven effective as anti-fertility agents in men. The flavonoid content in each tissue of *A. marina* is presented in Table 2 below.

Table 2. The potential of *A. marina* flavonoid compounds

No.	Bioactive Compound	Molecular Formula	*A. marina*				
			R	F	L	W	B
1	Butanoic acid, 3-methyl-, 3,7-dimethyl-6-octenyl ester	$C_{15}H_{28}O_2$					
2	Carbonic acid, propylundec-10-enyl ester	$C_{15}H_{28}O_3$	+				
3	cis-Z-.alpha.-Bisaboleneepoxide	$C_{15}H_{24}O$	+				
4	Chloroacetic acid, 2-tridecyl ester	$C_{15}H_{29}ClO_2$			+	+	+
5	Chloroacetic acid, 3-tridecyl ester	$C_{15}H_{29}ClO_2$	+	+	+	+	+
6	Chloroacetic acid, 4-tridecyl ester	$C_{15}H_{29}ClO_2$	+			+	+
7	Curdione	$C_{15}H_{24}O_2$			+		
8	Cyclopentadecanone	$C_{15}H_{28}O$		+			
11	Cyclooctyl N,N-dipropylphophoramidocyanidate	$C_{15}H_{29}N_2O_2P$	+				
12	Cyclohexene, 1-nonyl-	$C_{15}H_{28}$				+	
13	Cyclohexaneamine, N-(2,3,4-trimethylhex-3--enylidine)-N-OXIDE	$C_{15}H_{27}NO$	+	+		+	+
15	Dichloroacetic acid, 4-tridecyl ester	$C_{15}H_{28}Cl_2O_2$				+	

16	Methyl 10,11-tetradecadienoate	$C_{15}H_{26}O_2$		+	+	+	+
17	Methyl 11,12-tetradecadienoate	$C_{15}H_{26}O_2$	+	+			
18	Methyl 12,13-tetradecadienoate	$C_{15}H_{26}O_2$	+	+	+	+	+
19	Methyl 3-hydroxytetradecanoate	$C_{15}H_{30}O_3$		+			
24	Tetradecanoic acid, 2-hydroxy-, methyl ester	$C_{15}H_{30}O_3$		+	+	+	
26	trans-Z-.alpha.-Bisabolene epoxide	$C_{15}H_{24}O$	+	+			
31	3-Cyclohexylthiolane, S, S-dioxide	$C_{10}H_{18}O_2S$	+				
33	9-Borabicyclo[3.3.1]nonane, 9-(3-methoxy cyclohexyl)oxy-	$C_{15}H_{27}BO_2$	+	+	+	+	+
34	11,13-Dihydroxy-tetradec-5-enoic acid, methyl ester	$C_{15}H_{28}O_4$	+				
35	13-Borabicyclo[7.3.0]tridecane, 13-propoxy-, (Z)-or (E)-	$C_{15}H_{29}BO$	+	+	+	+	+
36	13-Tetradecynoic acid, methyl ester	$C_{15}H_{26}O_2$	+				
	Jumlah		**14**	**11**	**8**	**11**	**8**

R is root, FF is fruit and flower, L is leaf, W is wood, and B is bark.

Table 2 shows that *A. marina* is high potential as a natural anti-fertility agent due to its plant tissue's flavonoid content. Besides having a variety of flavonoids, *A. marina* is also very suitable as an anti-fertility herbal agent due to the presence of natural aphrodisiac compounds. Aphrodisiacs are substances that can increase sexual arousal and/or sexual pleasure [46]. Therefore, using *A.marina* as an anti-fertility agent is very appropriate because of its natural ability to minimize the side effects of decreased libido. Chandrakala and Rajeswari [19] reported that *A. marina* contains aphrodisiac compounds in its bark and roots.

A. marina has the potential to produce at least 36 types of flavonoids. Flavonoids are compounds that function as anti-fertility through hormonal and cytotoxic effects. Cytotoxic-cytologically, flavonoids produce Reactive Oxygen Species (ROS), which can damage the plasma membrane of spermatozoa [47, 48]. High levels of ROS in sperm can result in 40.88% of male patients experiencing infertility [49]. Oxidative stress will also reduce the activity of steroid hormones, which play a role in spermatogenesis [50].

Hormonally, the presence of flavonoids stimulates the formation of anti-fertility enzymes. It is in line with the report of Shukla and Dixit [51] have identified two unique enzymes, L-aspartate dehydrogenase, and trans-hexaprenyltranstransfe-rase which exhibit anti-fertility properties from 2 different metabolic pathways, namely nicotinic and nicotinamide metabolism and steroid biosynthesis. This enzyme is involved in steroid biosynthesis and nicotinic and nicotinamide biosynthesis; therefore, we can assume this enzyme is a potential target of new anti-fertility drugs.

Flavonoids are important bioactive compounds in the health sciences domain, primarily in the angiosperm plant group [52]. As an angiosperm plant, *A. marina* has a wide variety of flavonoids. The content of flavonoids in *A. marina* is much higher than several species of plants which are indicated to have potential as male anti-fertility agents, including *Caesalpinia sappan* which contains only one type of flavonoid [53]; *Piper ornatum* has three types of flavonoids [52]; and durian rind (*Durio zibethinus*) has nine types of flavonoids [48].

The many types of flavonoids contained in *A. marina* imply that the traditional use of the plant as an anti-fertility agent by coastal communities is in line with the scientific evidence that has been found. These findings can be the basis for research and development on using traditional herbal medicine into standardized herbal medicines or phytopharmaca. These findings can also be a scientific basis for efforts of emergency fertility control in the areas where accessibility and health facilities are limited. Emergency fertility control can also be applied to areas where traditional and religious beliefs cannot accept medical contraception.

A. marina is very potential as an herbal anti-fertility. However, the coastal community believes anti-fertility agents are only contained in the bark. The study's results prove that flavonoids, which act as anti-fertility agents, are not only found in the bark. Flavonoids are found in all tissues, with the highest type occurring in the root. The types of flavonoids in the bark are not as many as those in the roots, fruit, and wood. These findings can be the scientific basis for the sustainable utilization of mangrove resources by harvesting non-hazardous tissue to plant life such as leaves, flowers, fruit, or roots. Harvesting the bark could cut the phloem of vascular plants and disrupt the photosynthate distribution. Furthermore, open wounds on the bark have the potential to become a medium for pathogens penetration, especially bacteria, and viruses that are harmful to tree life [54].

The database generated from this study has provided an essential description of the content of bioactive compounds in *A. marina*. The results of this study provide an overview of the various benefits that may be obtained from the bioactive compounds of *A. marina*. One of the critical follow-up research in discovering herbal anti-fertility is the toxicity test and the effectiveness of various tissue extracts of *A. marina* as anti-fertility. This study can be performed both in vitro and in vivo examination. In vitro, examination can be done by testing it on cell culture, while in vivo examination can be done by testing it on experimental animals such as mice.

4. CONCLUSIONS

At least 49 bioactive compounds identified in various tissues of *A marina* were extracted using the GC-MS method and ethanol solvent. Of the 49 compounds, the bioactive found in *A. marina* tissue is primarily unique for each tissue. Flowers and fruit have a higher diversity of bioactive compounds, followed by wood, roots, leaves, and bark, with the number of bioactive being 21, 14, 13, 13, and 8, respectively. *A. marina* can produce 36 types of flavonoids. The group compounds that have been proven effective as male anti-fertility agents. It implies that *A. marina* has excellent potential as a male anti-fertility agent. These results reinforce the practice that coastal communities have carried out in utilizing *A. Marina*. The study results can be the basis for developing oral herbal contraception for men as an alternative contraceptive option in increasing men's participation in family planning.

So far, the plant part that is believed by the community to be male anti-fertility is the bark. However, it turns out that the types of flavonoids found in the bark are not as many as those found in roots (14), flowers and fruits (11), and wood (11). The types of flavonoids found in the bark are the same height as the leaves; each has only eight compounds. It implies that all parts of *A. Marina* has the potential as an anti-fertility agent. This finding is a new hope for the sustainable use of *A. Marina*,

because anti-fertility agents can be extracted from plant parts where harvesting does not endanger plant life, such as leaves, roots, flowers, and fruit.

However, the study only identified the content of flavonoid compounds that have the potential as anti-fertility agents. In the future, it is necessary to examine the toxicity and effectiveness of *A. Marina* extracts from various tissues as anti-fertility agents for animal tests.

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