Evaluation of phytochemical, antioxidant and anticancer activities of Indonesian mangroves herbal tea

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Abstract. Mangrove plants are potential raw materials for a variety of food and beverage items. Mangrove leaves can be processed into is mangrove herbal teas. Eight leaf samples of *Acanthus ilicifolius* (AI), *Avicennia marina* (AM), *Rhizophora apiculata* (RA), *Nypa fruticans* (NF), *Rhizophora mucronata* (RM), *Sonneratia caseolaris* (SC), *Sonneratia alba* (SA), and *Xylocarpus granatum* (XG) from Berau Regency, Kalimantan, Indonesia were investigated for phytochemical content (TPC and TFC), antioxidant activities (ABTS, DPPH, and FRAP), and anticancer activities (HepG2 and CaCo2 cancer cell line) have been done. We compared mangrove herbal teas to commercial black tea (*Camelia sinensis*/CS) for all activities. The result showed that the TPC value of CS was the highest and for TFC was in XG. Moreover, the antioxidant activities on ABTS possessed similar values except for AM, which had the lowest activities; on DPPH, SC and AI showed the highest activities among others; while SC and XG had the highest activities on FRAP. SC showed the highest activities on both cancer cell lines from the anticancer activities. We conclude that mangrove herbal teas from SC leaves have the potential to be functional food with great activities as antioxidants and anticancer agents.

1 Introduction

Mangroves are a unique plant family that includes trees, shrubs, ferns, and palms that grow and thrive in tropical and sub-tropical environments, exclusively in intertidal zones along coastal, estuarine, and riverine areas. They embody an intermediary habitat where the realms of the ocean, land, and freshwater intersect. Mangrove species are characterized by their

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ability to tolerate saline environments, anaerobic muddy soils, and the shifting conditions that are subsequently inundated and dry. A total of 110 mangrove species have been identified to date. Among them, 54 species belonging to 20 genera from 16 families are categorized as "true mangroves", meaning they are predominantly found in mangrove ecosystems [1, 2]. Southeast Asia is the region with the greatest concentration of mangroves, hosting around 75% of the global mangrove species. Among these species, Indonesia has the largest number with 45 species, followed by Malaysia with 36 species, and Thailand with 35 species [3].

Mangroves play a crucial role in the tropics and subtropics by providing coastal protection, preserving biological diversity, and safeguarding coral reefs and seagrass meadows [4]. Besides offering a source of food, timber, firewood, and beneficial natural chemicals, mangroves provide habitat, nutrients, and breeding grounds for 75% of all commercially fished species in tropical regions [3]. Their distinctive root systems effectively collect sediment, thereby preventing erosion and filtering out pollutants that would otherwise be carried into the sea. Mangroves, on average per hectare, also have the highest carbon content of tropical forests in the tropics. Upland tropical forests have significantly less carbon dioxide compared to mangrove. They also offer cost-effective opportunities for capturing and storing carbon [6, 7].

Furthermore, as one of the components of the forest ecosystem, mangrove is a renewable resource that can be processed to be a variety of food products. According to historical records, populations living in the coastal areas of Southeast Asia have traditionally used many species of mangrove trees for their daily meals, herbal medicines, and beverages [8-14]. Nevertheless, there is still room for improvement in terms of the variety of mangrove plant species, processing methods, and the types of food and drink products that may be created, taking into account the limitations of their knowledge.

Moreover, in many nations, such as Thailand, medicinal solutions derived from mangroves have been employed to alleviate infections, illnesses, and medical conditions. They are frequently ingested as teas, which are made by steeping dried plant components in hot water. Herbal teas and extracts made from the leaves of two mangrove species, namely *Pluchea indica* and *Acanthus ebracteatus*, are sold commercially. One example is Wanalee Co. Ltd., a herbal company that exports these products to other nations. This commercially available product of mangrove herbal teas indicates that it has economic value if managed correctly.

The therapeutic properties of mangrove herbal teas are linked to many phytochemicals that exhibit bioactive properties. The bark of Rhizophora trees contains a phenolic content ranging from 10% to 36%, which includes tannin, a type of polyphenol [15]. Polyphenols are a class of chemicals characterized by the presence of several phenolic hydroxyl (-OH) groups in their molecular structure. These functional groups are commonly found in plants [16]. The antioxidant properties of mangrove trees are attributed to the phenolic hydroxyl groups, which are responsible for protecting against oxidative stress. These groups produce hydrogen peroxide, which aids in the regulation of the immune system. Polyphenols also have been reported to reduce cancer, cardiovascular disease, diabetes type 2, pancreatitis, gastrointestinal problems, osteoporosis, and neurodegenerative disease [17]. Polyphenol have the powerful ability to eliminate harmful free radicals and its subsequent ability to prevent genetic mutations are beneficial in treating a variety of health disorders associated with modern lifestyles. These conditions include blood thinning effects, stomach ulcers, colorectal cancer, eye illness, and complications related to diabetes [18].

In this study, we observed antioxidant and anticancer activities from several species of mangrove leaves from Berau, East Kalimantan, Indonesia, as sources for mangrove herbal teas. From this data, we hope the potential of Indonesian mangroves as mangrove herbal teas for health purposes based on scientific evidence will arise.

2 Methods

2.1 Collecting samples

Eight types of mangroves were collected from Berau Regency, East Kalimantan, Indonesia. Mangrove types of RA, RM, and SA were found in Batu Putih District, while AM, NF, SC, XG, and AI types were taken from Tabalar District. Both Batu Putih District and Tabalar District have some different environmental characteristics. Mangrove ecosystems in Batu Putih District were growing on sandy substrate, but Mangrove ecosystems in Tabalar District thrived in estuary areas dominated by muddy substrate. The map of the sample collecting area can be seen in Figure 1.

Fig. 1. Map of samples collecting area in Berau Regency, East Kalimantan, Indonesia.

All collected leaves (Table 1) were dried using an oven at 40 ^{0}C for 24-48 hours. The dried leaves were then pulverized using a grinder using a particle size of 80 mesh. The samples were then kept in a dry place at room temperature and avoided light until used for the next analysis.

Table 1. The collected samples of mangroves leaves and black tea as a comparison

No.	Latin name	Sample code
1.	*Acanthus ilicifolius*	AI
2.	*Avicennia marina*	AM
3.	*Nypa fruticans*	NF
4.	*Rhizophora apiculata*	RA
5.	*Rhizophora mucronata*	RM
6.	*Sonneratia alba*	SA
7.	*Sonneratia caseolaris*	SC
8.	*Xylocarpus granatum*	XG
9.	*Camelia sinensis*	CS

2.2 Extraction

The extraction was prepared using the Loranty et al. [19] method with some modifications using the infusion method. The distilled water was used as the solvent (1:10 w/v). The hot plate was set at 70 ^{0}C, and the extraction was done in 10 minutes with the rotational speed of the magnetic steering bar at 100 rpm for homogenization. After 10 minutes, the extracts were filtered using a vacuum filter to extract wet bases. We applied the same extraction method to commercial black tea to compare tea-based beverage products.

To calculate the extraction yield, we used the oven-drying process to evaporate the water content in the extracts. We dried 5 mL of the extract in the oven at 105 ^{0}C overnight. The initial and final weights of the porcelain crucible were calculated to measure the extract yield.

2.3 Phytochemical content

2.3.1 Total phenolic content

Tang et al. [20] evaluated the total phenolic content with the Folin-Ciocalteu reagent using the same procedure. In 96 well plates, 25 L of the extract (1000 mg/L) was mixed with 25 L of Folin-Ciocalteu reagent solution (1:3 diluted with water) and 200 µL water was added. After that, incubate at room temperature for 5 minutes, add 25 µL 10% (w:w) sodium carbonate, and incubate again for 60 min at room temperature and dark area. A Tecan spectrophotometer plate reader (Tecan Group Ltd, Switzerland) was used to detect absorbance at 765 nm. TPC in samples was calculated using the gallic acid (0-250 mg/L) standard curve and reported as mg of gallic acid equivalents (GAE) per gram dry sample (mg GAE/g d.w.).

2.3.2 Total flavonoid content

Total flavonoid content was determined using the same method by Tang et al. [20]. For determination, 80 µL of the extract (1000 mg/L) was mixed with 80 µL 2% aluminium chloride and 120 µL 5% sodium acetate, incubated for 150 minutes at room temperature and dark area. The absorbance of flavonoid content was measured at an absorbance of 440 nm by a Tecan Spectrophotometer (Tecan Group Ltd, Switzerland). The total flavonoid content in samples was quantified from the quercetin (0-250 mg/L) standard curve and the value was expressed as mg of quercetin equivalent per g (mg QE/g d.w.)

2.4 Antioxidant activities

2.4.1 ABTS assay

A method for measuring ABTS scavenging activity described by [20], and we modified the calculation of radical scavenger activities with percent inhibition [20]. 5 mL of ABTS (2,2-Azino-bis-3-Ethylbenzothiazoline-6-Sulfonic Acid) (7mM) was combined with 88 L of K2S2O8 (140mM) and incubated for 16 hours at room temperature and in the dark. The ABTS+ radical solution was diluted using ethanol until it had an absorbance of 0.7. Concentration series (5, 10, 20, 30, 40, and 50 ppm) samples were employed. The 10 µL sample was put into the well along with 290 µL of ABTS solution and in the dark incubated for 6 minutes at room temperature. A Tecan microplate reader (Tecan Group Ltd, Switzerland) was used to measure the absorbance of radical scavenger ABTS assay the

sample at a wavelength of 734 nm. The percentage inhibition of free radical scavenging activity was calculated using the following equation:

$$\% \text{ inhibition} = (A-B)/A \times 100 \quad (1)$$

where A = absorbance of the blank sample, and B = absorbance of the extracts [20].

2.4.2 DPPH assay

A method described to evaluate DPPH scavenging activity, and we modified the calculation of radical scavenger activities with percent inhibition [20]. A 40 µL of extract or standard was added to 40 µL of DPPH in methanolic solution (0.1 mM) and incubated the mixture in the dark at 30 ^{0}C for 30 minutes. A Tecan microplate reader (Tecan Group Ltd, Switzerland) was employed to measure the absorbance of radical scavenger activities in the sample at 517 nm. The percentage inhibition of free radical scavenging activity was calculated using the same equation as the ABTS assay (2.4.1)

2.4.3 FRAP reducing power

The FRAP assay was conducted using the methodology outlined [20]. The FRAP solution was made by combining a 300 mM solution of sodium acetate, a 10 mM solution of TPTZ (2, 4, 6-tripyridyl-s-triazine), and a 20 mM solution of Fe[III] in a ratio of 10:1:1. A 20 µL sample or reference solution was introduced into 280 µL of produced FRAP and subjected to incubation at 37 ^{0}C for 10 minutes. The measurement of absorbance was conducted at a wavelength of 593 nm using a Tecan Spectrophotometer, manufactured by Tecan Group Ltd in Switzerland. The FRAP activity values were transformed into milligrams of ascorbic acid equivalents per gram (mg AAE/g dw) by utilizing a standard curve of ascorbic acid that spanned from 0 to 250 milligrams per liter (mg/L).

2.5 Anticancer activities

2.5.1 Cell culture

The colorectal cancer cell line CACO-2 (ECACC: 86010202) and hepatocarcinoma cell line Hep-G2 (ECACC: 85011430) were used for this experiment. The CACO-2 and Hep-G2 cell lines were cultured in DMEM (Dulbecco's modified Eagle's medium) containing 10% fetal bovine serum (FBS) and 1% antimycotic antibiotic, incubated in a 37 °C incubator with CO_2 levels 5%.

2.5.2 Viability assay (MTT)

Anticancer activity was measured by determining the viability of cells using the MTT described by Kumar et al. [21]. The cells that were 80% confluent were planted in 96-well plates at 10.000 cells/well with a volume of 100 µL per well, then incubated for 24 hours. After that, the treatment of cells using 100 µL of the extract was incubated for 24 hours in a 5% CO_2 37 ^{0}C incubator. Then, observe the cells using an inverted microscope. After being treated and incubated for 24 hours, the culture medium was removed 100 µL, and then 10 µL of MTT solution was added to each well. Hereafter, incubation for 2-4 hours in a 5% CO_2 37 ^{0}C incubator. Then, observe the cells under an inverted microscope to see the formed formazan. The cell medium was discarded until 50 µL remained, and the formazan was

dissolved using 100 µL DMSO. The absorbance value of cells stained with MTT was measured using a Tecan microplate reader (Tecan Group Ltd, Switzerland) with a wavelength of 570 nm. The viability was measured using the calculation as follows:

$$\% \text{ viability} = (\text{Abs treated cells}/\text{Abs untreated cells}) \times 100\% \quad (2)$$

2.6 Statistical analysis

The values were reported as the mean ± standard deviation, with each sample being replicated at least three times. Linear regression for the standard was also performed in Microsoft Excel 2023.

3 Results and Discussion

3.1 Extract yield

The extraction of mangrove herbal teas was done using the infusion method. The distilled water was used as the solvent (1:10 w/v) with moderate heating at 70 ºC and homogenization at 100 rpm. This extraction method showed that *Xylocarpus granatum* and *Camelia sinensis* (as a reference) had the highest extract yield (Figure 2). This result can be caused by the phytochemical content in *Xylocarpus granatum* and *Camelia sinensis*, which have the same polarity as water, such as phenolics, flavonoids, alkaloids, and tannins. Hence, the highest yield among the other extracts indicates it. The different accumulation of yield mangrove herbal teas is based on several factors such as species, ages, growth location, and phenological cycle [22, 23].

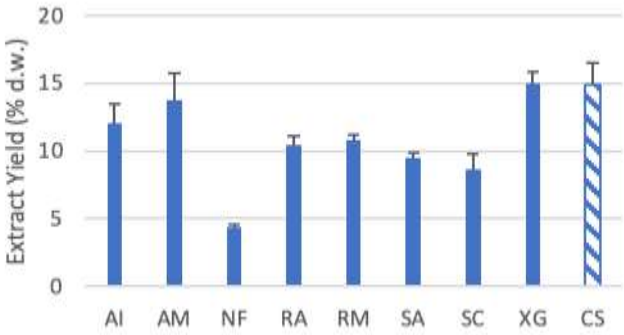

Fig. 2. Extract yield from the different extraction of mangrove herbal teas and black tea; *Acanthus ilicifolius* (AI); *Avicennia marina* (AM); *Nypa fruticans* (NF); *Rhizophora apiculata* (RA); *Rhizophora mucronata* (RM); *Sonneratia alba* (SA); *Sonneratia caseolaris* (SC); *Xylocarpus granatum* (XG); *Camelia sinensis* (CS)

3.2 Phytochemical content

Phenolics and flavonoids are natural compounds in mangrove herbal teas, and both have therapeutic agents such as antioxidant, antibacterial, anticancer, anti-inflammatory, and cardioprotective effects. In this study, the highest total phenolics and flavonoid content of mangrove herbal teas was *Camelia sinensis* (as a reference), followed by *Rhizopora apiculata* and *Xylocarpus granatum* (Figure 3). Total phenolics and flavonoids content from *Rhizophora apiculata* was higher than the previous study, which reported the phenolics and

flavonoids content water extract were determined at 53.24 ± 0.02 mg GAE/g extract and 44.18 ± 0.08 mg QE/g extract [24], *Xylocarpus granatum* total phenolics has been reported in previous study 6,163 mg GAE/g [25]. Different types of mangroves also showed different types of phytochemical content. However, there are common types of phytochemical compounds found in mangrove species which are terpenoids (16.25%), tannins (12.5%), steroids (10.0%), alkaloids (9.38%), saponins (8.75%), flavonoids (8.75%), and glycosides (8.13%) [26]. The phytochemical content is also related to the pharmacological activities, for example, high phenolic content possesses high antioxidant activities.

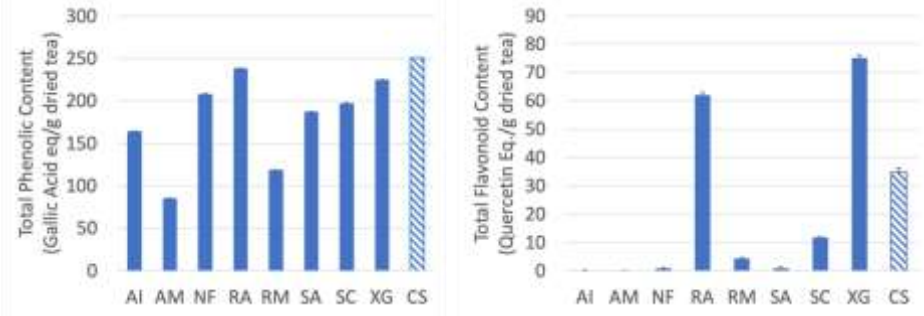

Fig. 3. Total phenolic and total flavonoid content from the different extracts of mangrove herbal teas and black tea; *Acanthus ilicifolius* (AI); *Avicennia marina* (AM); *Nypa fruticans* (NF); *Rhizophora apiculata* (RA); *Rhizophora mucronata* (RM); *Sonneratia alba* (SA); *Sonneratia caseolaris* (SC); *Xylocarpus granatum* (XG); *Camelia sinensis* (CS)

3.3 Antioxidant activities

The antioxidant activities of mangrove herbal teas were determined using ABTS, DPPH, and FRAP assay. The result showed that on the ABTS assay, the inhibition activities of all extracts were the same. Meanwhile, on the DPPH assay, *Sonneratia caseolaris* and *Acanthus ilicifolius* showed higher inhibition than other extracts. Moreover, on the FRAP assay, the highest activities were shown by *Xylocarpus granatum* and *Camelia sinensis* (Figure 40. In a previous study [27-28], *Sonneratia caseolaris* and *Achanthus ilicifolius* ethanol leaf extract also showed potent antioxidant activity against DPPH radicals. In the FRAP assay, there are no reports on the antioxidant activity of *Xylocarpus granatum* leaves, although extracts from its seeds and roots have been reported to be potent [29]. The antioxidant potential of *Sonneratia caseolaris, Acanthus ilicifolius*, and *Xylocarpus granatum* may be attributed to their phytochemical compounds. *Sonneratia caseolaris* reportedly has a compound such as azelaic acid, aspirin, isovitexin, luteolin, luteolin 7-O-b-glucoside cymaroside, and quercitrin. *Acanthus ilicifolius* has a compound such as methylapigenin7-o-β-D-glucuronate-flavone glycosides, bisoxazolinone, 2-benzoxazolinone, and coumaric acid derivative-acancifoliuside. *Xylocarpus granatum* has compounds such as catechin, epicatechin, procyanidins, xyloccensin, and gedunin [27, 30]. The differences in antioxidant capacity among mangrove herbal teas can be caused by a bioactive compound in the extract and the mechanism of antioxidants that are affected by those compounds. The mechanism of antioxidants from the ABTS and DPPH assays is quite similar, which involves donating electrons or hydrogens to deactivate radical species. The ABTS assay has more advantages, as it has the ability to detect samples with a broader pH range and able to determine the antioxidant activity of hydrophilic and hydrophobic samples. The difference from the previous assay is that the mechanism of the FRAP assay is a reduction of ferrous ions [31-33].

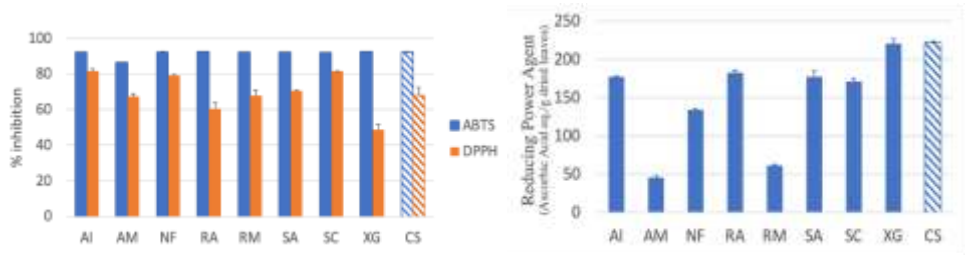

Fig. 4. Antioxidant activities of ABTS, DPPH and FRAP assay from the different extract of mangrove herbal teas and black tea; *canthus ilicifolius* (AI); *Avicennia marina* (AM); *Nypa fruticans* (NF); *Rhizophora apiculata* (RA); *Rhizophora mucronata* (RM); *Sonneratia alba* (SA); *Sonneratia caseolaris* (SC); *Xylocarpus granatum* (XG); *Camelia sinensis* (CS)

3.4 Anticancer activities

The anticancer activities of mangrove herbal teas in this study are using colorectal cancer (CACO-2) and hepatocarcinoma (Hep-G2) cell lines. The result showed that *Sonneratia caseolaris* has the highest activity in both cancers, followed by *Camelia sinensis* (Figure 5). *Soneratia caseolaris,* also referred as mangrove apple, is a readily accessible plant with a multitude of uses due to its physical and chemical qualities. It is non-toxic and may be easily cultivated. In a previous study [34], *Sonneratia caseolaris* reportedly has an isolated compound known as 3′,4′,5,7-Tetrahydroxy flavone that has the potential against the proliferation of human hepatoma SMMC-7721 cells line. The other study reports that *Sonneratia caseolaris* has many bioactive compounds like flavonoids, steroids, triterpenoids, benzene-carboxylate derivatives, alkaloids, pectin, fatty acids, tannins, and sugars such as a flavone, luteolin, and luteolin 7-O-b-glucoside (cynaroside) as therapeutic agents for antiseptic, antitussive, antipyretic, astringent, hemostatic activities, antibacterial, pesticidal, antifungal, insecticidal, antidiabetic, anticancer and anti-cholesterol activities [35].

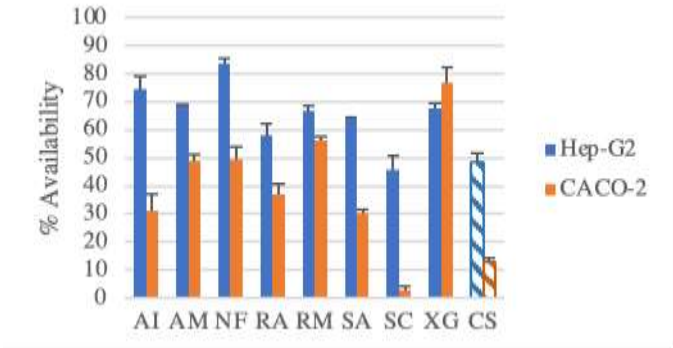

Fig. 5. Viability of two types of cancer cell lines Hep-G2 and CACO-2 by treatment of different extracts of mangrove herbal teas and black tea; *Acanthus ilicifolius* (AI); *Avicennia marina* (AM); *Nypa fruticans* (NF); *Rhizophora apiculata* (RA); *Rhizophora mucronata* (RM); *Sonneratia alba* (SA); *Sonneratia caseolaris* (SC); *Xylocarpus granatum* (XG); *Camelia sinensis* (CS).

4 Conclusion

The phytochemical content of screened mangrove herbal teas on the TPC value showed CS>RA>XG>NF>SC>SA>AI>RM>AM. Meanwhile, the TFC value showed

XG>RA>CS>SC>RM>SA>NF>AI=AM. The antioxidant activities of the mangrove herbal teas on ABTS possessed similar values. However, on DPPH, SC and AI showed the highest activities. While SC and XG had the highest activities on the FRAP assay. SC tea showed the highest activity on both cancer cell lines Hep-G2 and CACO-2. The mangrove herbal teas from SC leaves has the potential to be a functional food with great activities as an antioxidant and anticancer.

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