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Kertas Asli/*Original Articles*

Antimicrobial Activities of Mangrove Species in Southeast Asia: A Systematic Review

(Aktiviti Antimikrob Spesies Bakau di Asia Tenggara: Tinjauan Sistematik)

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ABSTRACT

Antimicrobial resistance in Southeast Asia is a macro-level health dilemma that may cause substantial casualties annually. Fortunately, Southeast Asian mangroves are potent reservoirs of bioactive compounds with antimicrobial properties in correlation to their traditional usage. Hence, this study aimed to systematically review studies concerning antimicrobial activities of mangroves in Southeast Asia as well as provide a technological overview of its prospective use in pharmaceutical industry applications through patents. Through the PRISMA protocol, the search for peer-reviewed studies originated from Southeast Asia and published between 2010 to 2022 were conducted over databases such as CORE, Google Scholar, PubMed (MedLine), Science Direct, Semantic Scholar, Scopus, and Web of Science. Additionally, a patent search was also performed on the Espacenet Patent Search, Google Patents, National Institute of Industrial Property, and United States Patent and Trademark Office. The studies and patents were collated on Mendeley Reference Manager as well as tabulated and assessed on Microsoft Office Excel 2016. After the four-phase screening, 59 studies and one patent regarding antimicrobial activities of Southeast Asian mangroves passed the criteria for the systematic review. It was inferred that Southeast Asia constitutes potentially most species-diverse mangroves with highly varied antimicrobial properties and can form synergism with drugs. The existing studies and patents may provide enlightenment on the future path of studies and inventions which must be continually substantiated in animal and clinical experiments for prospective pharmaceutical industry use. In this way, mangroves can be conserved while antimicrobial resistance and anthropogenic activities can be lowered.

Keywords: Mangroves; antimicrobial activities; Southeast Asia; antimicrobial resistance; Systematic review

ABSTRAK

Kerintangan antimikrob di Asia Tenggara merupakan dilema kesihatan pada aras makro yang menyumbang kepada kematian setiap tahun. Pokok bakau Asia Tenggara berpotensi sebagai reservoir untuk bahan bioaktif bersifat antimikrob yang telah diguna pakai secara tradisional. Oleh itu, kajian ini bertujuan untuk meneliti kajian lepas secara bersistematik berkenaan dengan aktiviti antimikrob pokok bakau di Asia Tenggara dan juga teknologi penggunaannya dalam industri farmaseutikal melalui paten. Melalui protocol penyaringan PRISMA, pencarian penerbitan berwasit dari Asia Tenggara sekitar 2010 hingga 2022 telah dilakukan melalui database seperti CORE, Google Scholar, PubMed (MedLine), Science Direct, Semantic Scholar, Scopus, and Web of Science. Tambahan lagi, pencarian paten melalui Espacenet Patent Search, Google Patents, National Institute of Industrial Property, and United States Patent and Trademark Office juga dilakukan. Dapatan pencarian diselaraskan dengan Mendeley Reference Manager, kemudiannya dijadualkan dan dinilai dengan Microsoft Office Excel 2016. Setelah empat fasa penyaringan, 59 kajian dan satu paten berkenaan aktiviti antimikrob pokok bakau Asia Tenggara didapati menepati kriteria penyaringan. Asia Tenggara didapati mempunyai spesies pokok bakau yang meluas dan bersifat antimikrob yang dapat menunjukkan nilai sinergi dengan ubatan. Kajian dan paten yang sedia ada dapat merupakan rujukan bagi kajian serta inovasi pada masa depan. Kajian dan inovasi tersebut perlu dilengkapi dengan ujian pada model haiwan serta klinikal agar dapat diaplikasikan dalam industri farmaseutikal. Dengan itu, pokok bakau dapat dipelihara dan kejadian rintang antimikrob dan aktiviti antropogenik dapat dikurangkan.

Kata kunci: Bakau; aktiviti antimikrob; Asia Tenggara; kerintangan antimikrob; tinjauan bersistematik

INTRODUCTION

Antimicrobial resistance (AMR) is a progressing global health and development threat because of the resistance of microorganisms which consist of fungi, bacteria, parasites, and viruses to formerly useful antimicrobial drugs as therapeutics for infection. AMR is also of global concern since based on the estimation of the United Kingdom (UK) Department of Health by 2050, it will contribute to 10 million deaths annually worldwide (O'Neill 2016). In Southeast Asia, the entire region was assessed to be at high risk of surfacing and disseminating antibiotic resistance among individuals (Chereau et al. 2017). With the advent and increased rate of antimicrobial resistance of microorganisms to commercially available drugs, it is vital to explore novel potential sources of drugs.

Different kinds of plants have been extensively studied to discover antimicrobial compounds (Chandra et al. 2017). Fortunately, the mangroves in Southeast Asia are prospective reservoirs of natural products such as bioactive secondary metabolites with highly varied antimicrobial properties (Patra & Thatoi 2011). Mangroves are characterized as a coastal wetland ecosystem that contained diverse species of shrubs, herbs, and trees capable of growing in a seawater setting (Doydee & Buot 2010; Lillo & Buot 2016; Smith & Smith 2004). However, around 35% of the world's mangrove forest area has been eradicated as reported from 1980 to 2001 (Food and Agriculture Organization 2003; Lillo & Buot 2016; Valiela et al. 2001). Together with mangrove associates, they are affected by indirect anthropogenic factors such as progressing commercialization, climate change, destruction, and over-exploitation (Lillo & Buot 2016).

As the mangrove areas declined continually along with the emergence and progressive cases of antimicrobial resistance, it is imperative to explore the Southeast Asian mangroves to further combat drug resistance caused by pathogens as well as conserve the mangrove ecosystem. Hence, this study aimed to systematically review the existing studies and patents on the antimicrobial activities exhibited by various species of mangroves in Southeast Asia and their synergistic effects with drugs. It also intended to evaluate the methodological quality of studies regarding mangrove species with antimicrobial action as well as present the published patents which may entail prospective industrial and pharmaceutical applications in controlling the growth of microbes.

METHODS

This qualitative systematic review was carried out by following the four-phase flow diagram of the PRISMA Statement to perform the search for suitable scientific studies (Moher et al. 2009).

SEARCH STRATEGY

Various scientific databases involving CORE, Google Scholar, PubMed (MedLine), Science Direct, Scopus, Semantic Scholar as well as Web of Science, were mined for published studies between 2010 and 2022 with no time limit, written in the English language, and thoroughly reviewed afterward. The search method utilized the following keywords: "antibacterial", "antiviral", "antifungal", "antiprotozoal", "anthelminthic", "antimicrobial activity", "mangrove", "mangrove plant extracts", "synergistic activity", and "industry", along with names of each country located in Southeast Asia. On the other hand, the utilized patent databases were Espacenet patent search (EPO), Google Patents, National Institute of Industrial Property (INPI), and the United States Patent and Trademark Office (USPTO). Within these databases, the included patents focused on Southeast Asian mangroves with antimicrobial activities and publication years further than or equal to 2010 as well as with documents written in the English language. Otherwise, the patents were not included in the latter screening phase.

Two independent reviewers screened the title of the entire identified published studies and patents for correlation with the research aim and location verification. Once the title agreed with the inclusion criteria, the reviewers proceeded to carefully assess the abstracts of the studies and patent documents. On the other hand, articles that were deemed qualified for the review, or in case skeptical, proceeded further into full-text reading. Moreover, group discussions were applied to resolve any discrepancies that may occur. For additional studies, hand-searching was conducted as well for the reference of all included studies (Chassagne et al. 2021; dos Santos et al. 2017; Hlashwayo et al. 2020).

INCLUSION AND EXCLUSION CRITERIA

The abstracts and titles of all published studies and patents were subjected to manual screening to eliminate those which did not correlate with the research topic. The specific inclusion criteria for the studies included papers published between 2010 and 2022 that dwelled on Southeast Asia countries, primary peer-reviewed articles, methodology with effective extraction procedures and antimicrobial assays with Minimum Inhibitory Concentration (MIC) or Half-maximal Inhibitory Concentration (IC_{50}) values for plant extracts, as well as papers published in the English language with the accessible full-text article. On the other hand, the specific exclusion criteria for studies involved published papers before 2010 and dwelled on other parts of Asia, all grey literature and articles, ineffective methods for extraction, ineffective antimicrobial assays with lacked MIC or IC_{50} values for plant extracts, and articles merely issued in non-English languages.

In terms of patents, the inclusion criteria involved published patent documents in the English language that dwelled in Southeast Asia countries and with publication years between 2010 and 2022. The exclusion criteria were contrary to the stated criteria for the included patents.

DATA EXTRACTION

The data from eligible studies and patents regarding the antimicrobial activities of Southeast Asian mangroves were collated independently by two reviewers. In case of missing data, the authors of the extracted studies were contacted (dos Santos et al. 2017). For the analysis of the data, the collated information from studies and patents search was organized, maintained, and visualized in Microsoft Excel spreadsheet form. On the other hand, Mendeley Reference Manager was employed for the organization of all studies, patents, and references gathered.

ASSESSMENT OF RISK OF BIAS

The methodological quality of each included study was evaluated by the reviewers independently (dos Santos et al. 2017). Hence, the risk of bias was appraised based on the description of the studies in terms of the parameters involved in extraction and antimicrobial assay methods. The studies garnered a "Yes" on a specific parameter as the authors presented that parameter; while a "No" was received by a study since the specific parameter is impossible to find in the data of certain authors. On the other hand, a high risk of bias will be indicated in the studies that presented one to three items, a medium risk of bias will be implied for four or five presented items, and a low risk of bias will be indicated in the studies that presented six to eight items (Cocco et al. 2015). However, since the current study contains 16 parameters for the assessment of the methodological quality of the extracted studies, the interpretation of the level of risk of bias was modified. A high risk of bias was indicated in the studies that presented one to six parameters, a medium risk of bias was implied for seven to 10 parameters that were presented, and a low risk of bias was indicated in the studies that positively presented 11 to 16 items.

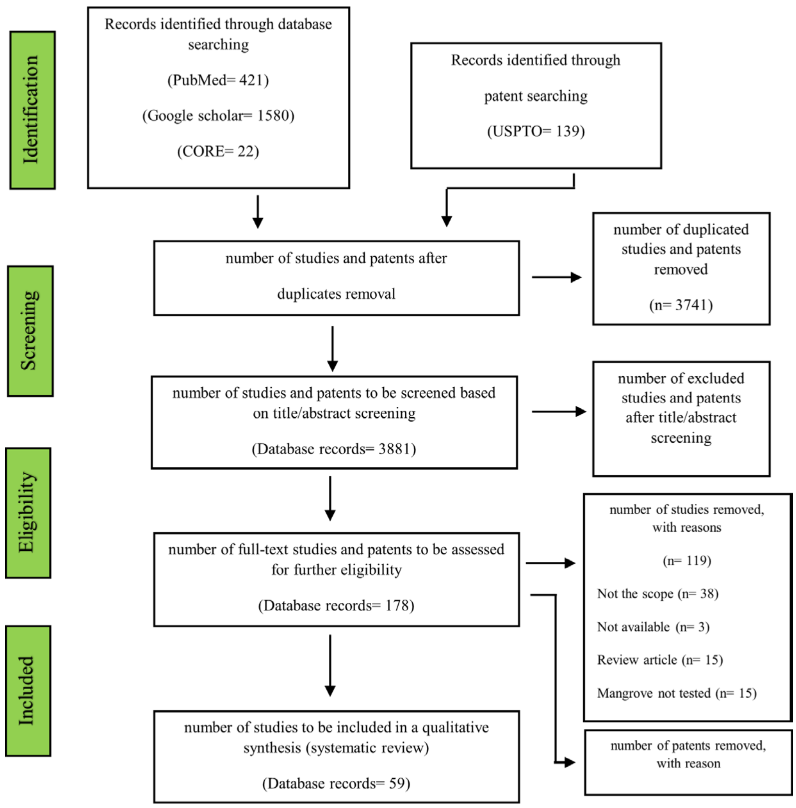


FIGURE 1. PRISMA flow diagram of study selection for the systematic review of antimicrobial activities of mangroves species from Southeast (SE) Asia after data gathering

RESULTS

STUDY SELECTION

A total of 6651 studies were identified from the data mining in various databases. Through the screening phase, the collated data were subjected to deduplication resulting in 3881 studies. Moreover, these studies proceeded to title and abstract screening which resulted in 178 remaining studies for further eligibility assessment. The full-text screening phase revealed that 119 studies were removed due to the reasons provided in Figure 1. As a result of this thorough assessment, 59 articles were included in the final set of studies to be reviewed.

Furthermore, in terms of patent searching, 1012 patents were retrieved and after duplicate removal, 41 patents remained. Meanwhile, 31 patents were excluded since they were not associated with mangroves and antimicrobial activity. Hence, 10 patents remained for eligibility screening. Finally, only one (1) patent was considered in this review.

STUDY CHARACTERISTICS

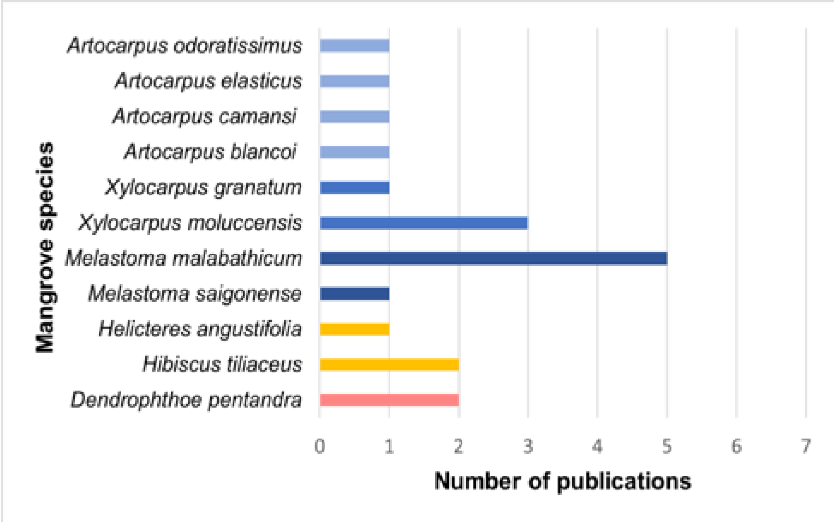
The systematic matrix on the antimicrobial activities of Southeast Asian mangroves is constructed which corresponded to the study characteristics of the final included articles after the data extraction procedure. It was hypothesized in this review that several bioactive compounds within mangrove extracts could lessen and control the growth of microorganisms. This is justified by the 57 in vitro antimicrobial studies concerning the use of mangrove extracts and tested 78 microorganisms (27 Gram-positive and 31 Gram-negative bacteria, 15 fungi, 2 protozoa, and 3 viruses). However, it can be observed that two (2) published studies did not report positive antimicrobial activity at all (Sibero et al. 2020; Sirichoat et al. 2021).

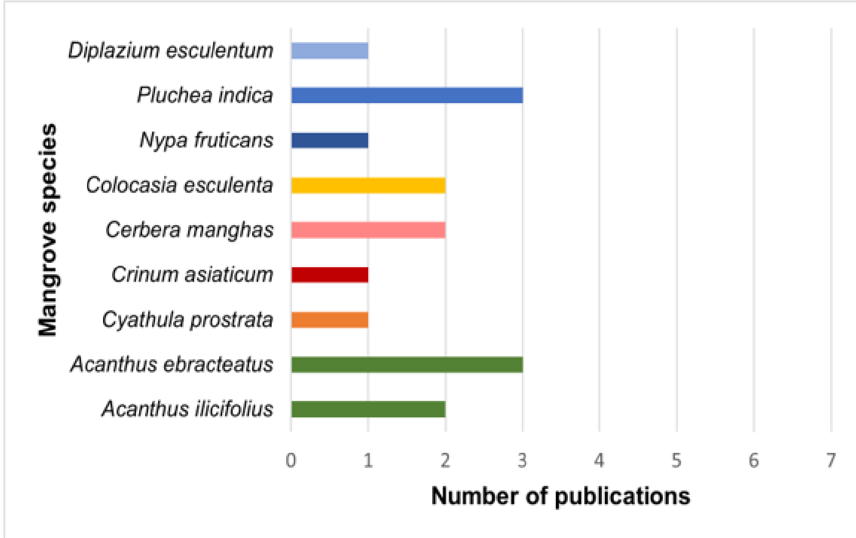
In general, the sample size used in antimicrobial tests is small and most of the studies applied triplicate samples per test group. Furthermore, the frequent exposure time to most antimicrobial tests is one day (24 h). Within these tests, some studies (n=29) did not employ either one or both of the control groups. This information entails the limitation of the research design in their in vitro studies.

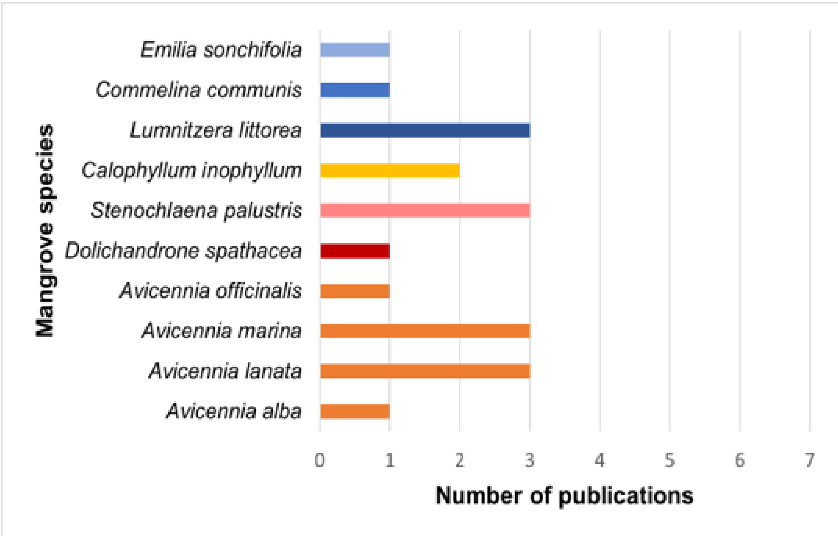
SOUTHEAST ASIAN MANGROVES SPECIES AND THEIR DISTRIBUTION

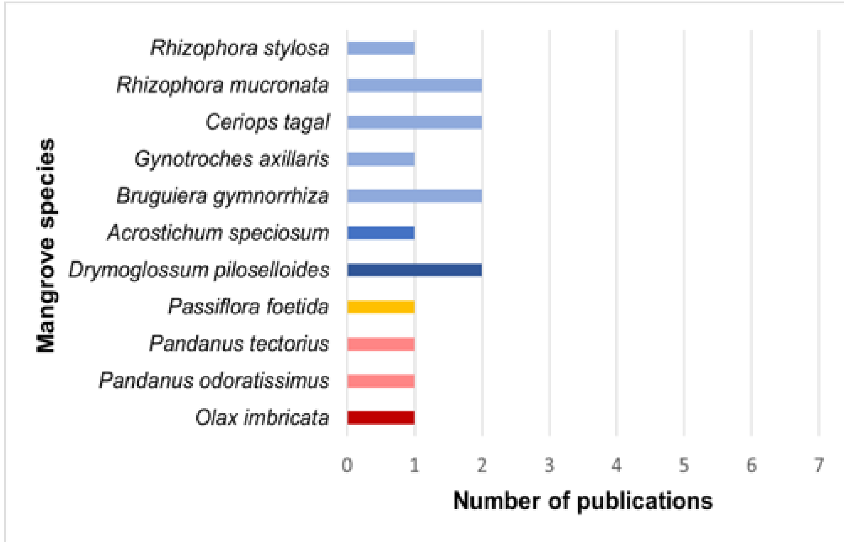
The distribution of mangroves tested for their antimicrobial activity throughout Southeast Asia is illustrated in Figure 2. Based on the figure, Indonesia has the highest tested mangrove (n=38) which was followed by Malaysia with 13 mangroves tested, then Thailand with 10 mangroves species tested. In contrast, the countries of Brunei, Singapore, and Timor Leste have no reported studies since the articles from the said countries did not pass the inclusion criteria.

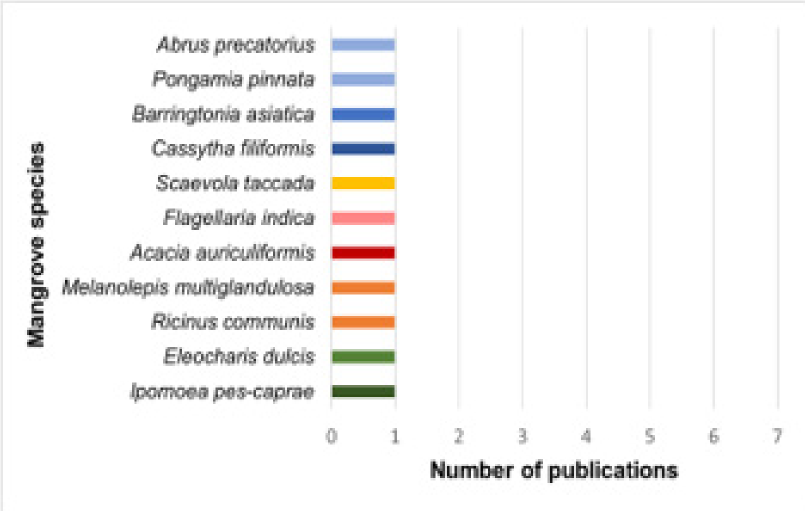
FIGURE 2 The distribution of tested Southeast Asian mangrove species by country of origin with reference from the final included studies


Mangrove species
Artocarpus odoratissimus
Artocarpus elasticus
Artocarpus camansi
Artocarpus blancoi
Xylocarpus granatum
Xylocarpus moluccensis
Melastoma malabathicum
Melastoma saigonense
Helicteres angustifolia
Hibiscus tiliaceus
Dendrophthoe pentandra
0 1 2 3 4 5 6 7
Number of publications


Mangrove species
Diplazium esculentum
Pluchea indica
Nypa fruticans
Colocasia esculenta
Cerbera manghas
Crinum asiaticum
Cyathula prostrata
Acanthus ebracteatus
Acanthus ilicifolius
0 1 2 3 4 5 6 7
Number of publications


Mangrove species
Emilia sonchifolia
Commelina communis
Lumnitzera littorea
Calophyllum inophyllum
Stenochlaena palustris
Dolichandrone spathacea
Avicennia officinalis
Avicennia marina
Avicennia lanata
Avicennia alba
0 1 2 3 4 5 6 7
Number of publications


Mangrove species
Rhizophora stylosa
Rhizophora mucronata
Ceriops tagal
Gynotroches axillaris
Bruguiera gymnorrhiza
Acrostichum speciosum
Drymoglossum piloselloides
Passiflora foetida
Pandanus tectorius
Pandanus odoratissimus
Olax imbricata
0 1 2 3 4 5 6 7
Number of publications



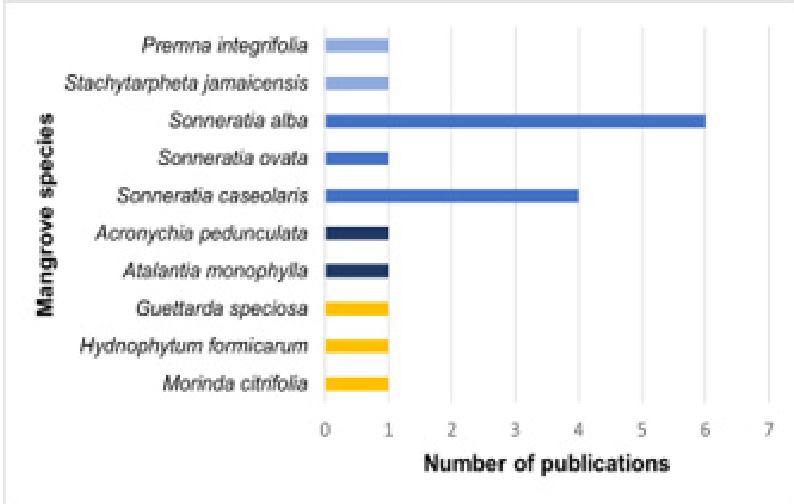


FIGURE 3. Mangrove plant species by the number of publications. The entire figure constitutes six bar graphs and the same bar color within each graph denotes species with the same family

Furthermore, within the reported 59 antimicrobial-related studies that utilized mangroves, a total of 62 mangroves species from Southeast Asia were examined for in vitro activity against pathogenic microorganisms. It was deemed that the mangroves species belong to 39 families. Mangrove plants from the Rhizophoraceae family were the most common with five (5) species. Other families such as Avicenniaceae and Moraceae each represented four (4) species of mangroves. Moreover, *Sonneratia alba* (n=6), *Melastoma malabathricum* (n=5), and *Sonneratia caseolaris* (n=4) were the three most studied species (Figure 3). Both of the most studied *Sonneratia* species are classified as true mangroves with shrub to tree formation while *M. malabathricum* is a mangrove-associate with shrub to tree formation as well.

Out of 62 mangroves, a total of 51 species tested positive for antimicrobial activity while 11 species were reported with no inhibitory action against microorganisms. These include *Dolichandrone* spathacea and *Lumnitzera littorea* (Kaewpiboon et al. 2012), *Atalantia monophyla* (Sirichoat et al. 2021), and *Rhizophora mucronata* (Sibero et al. 2020). To add, other mangroves with no inhibitory action are *Acanthus ebracteatus* Vahl, *Artocarpus elasticus* Reinw. ex Blume, *A. odoratissimus* Blanco, *Commelina communis* (L.), *Cyathula prostrata* (L.) Blume, *Emilia sonchifolia* (L.) DC. ex, and *Helicteres angustifolia* L. (Kudera et al. 2021). Hence, those species are not a potential source of antimicrobial compounds.

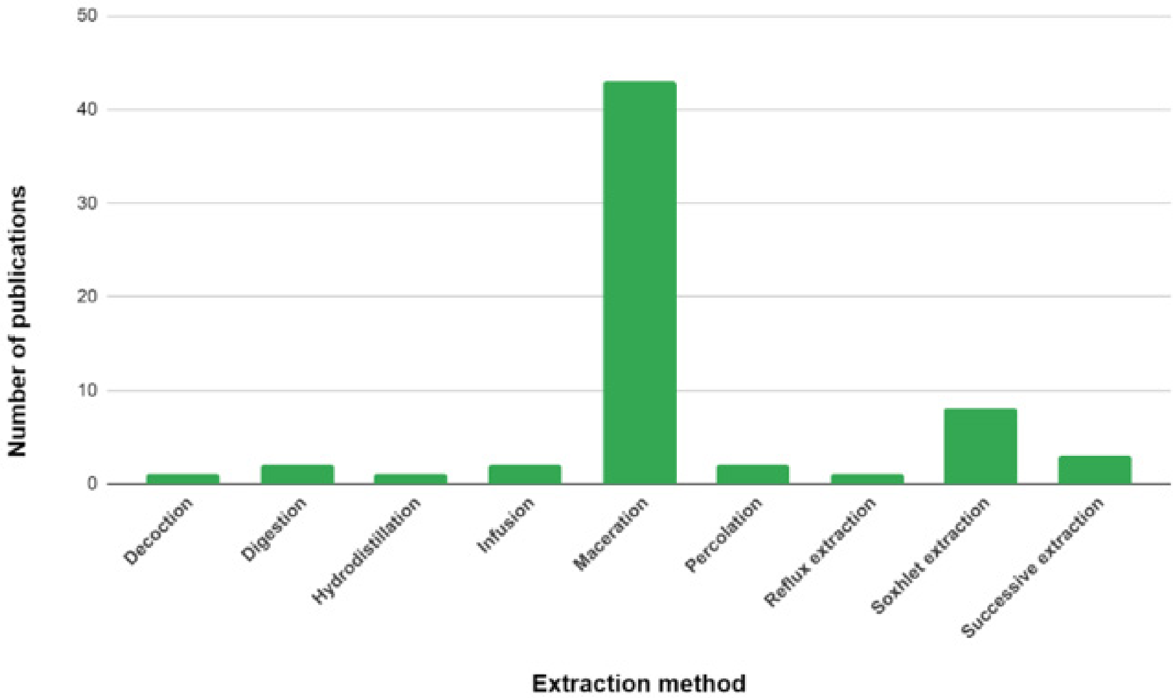
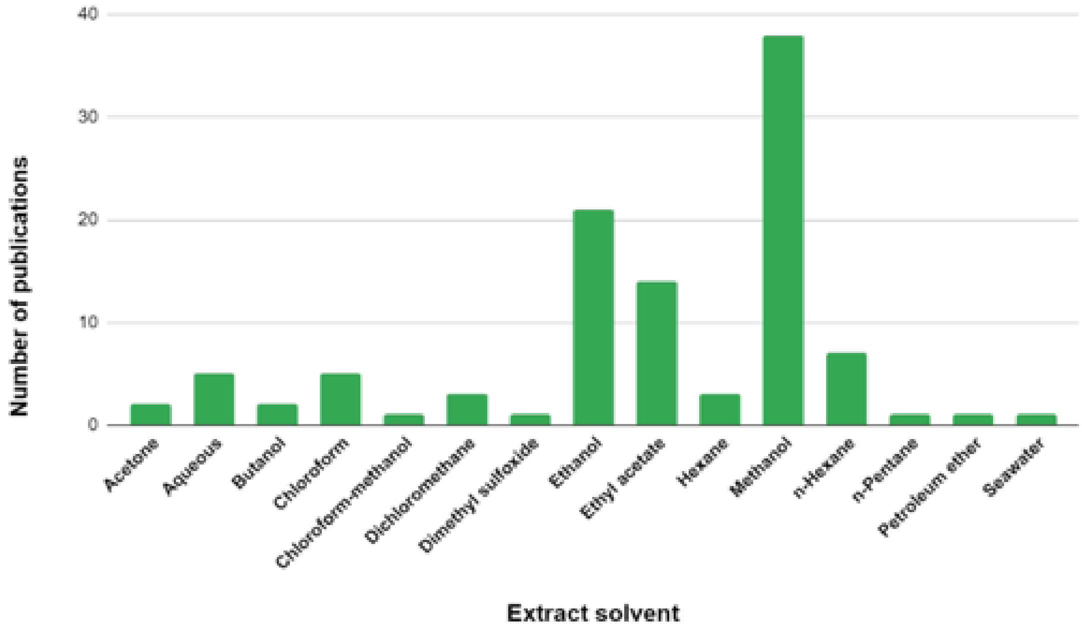


FIGURE 4. Frequency of extraction methods employed for mangrove extracts by publication number

(A)



(B)

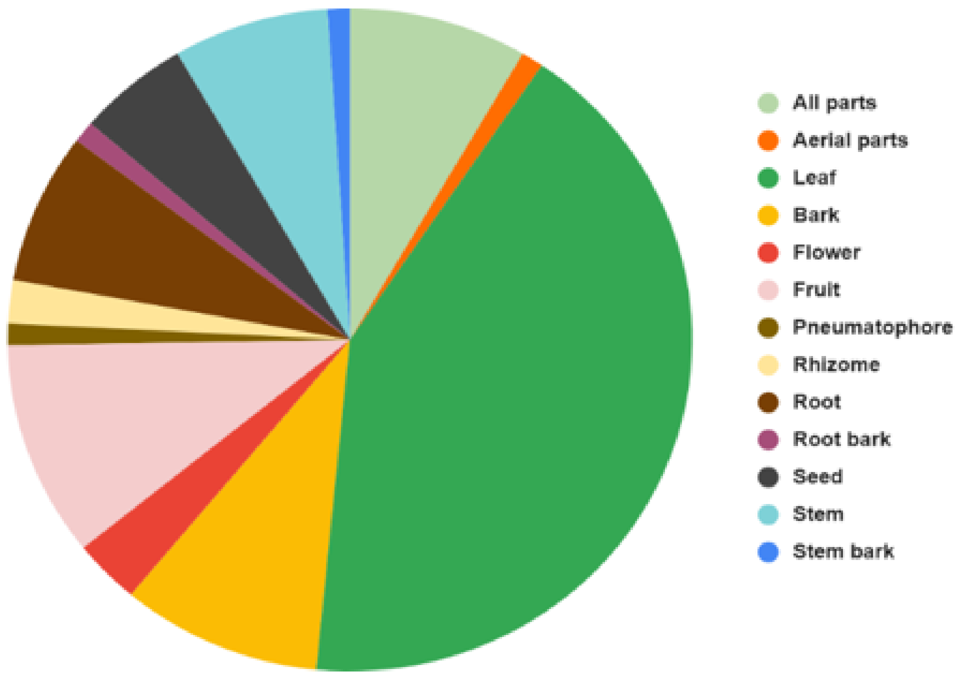


FIGURE 5 (A). Frequency of solvents utilized for mangrove extracts by the publication number and (B) Southeast Asian mangroves plant tissue tested for antimicrobial activity

MANGROVE PARTS AND EXTRACTION METHODS EMPLOYED

The bar graph in Figure 4 displayed the various extraction methods utilized by 59 reviewed studies. It revealed that maceration is the most employed since 43 studies included it in their methodology. On contrary, the least extraction methods used are decoction, hydrodistillation, and reflux extraction (n=1). In conducting an extraction of plant extracts, it is accompanied by a solvent and a plant tissue of interest. The extraction solvent with the highest frequency is methanol (n=38) (Figure 5A) while the leaf is the most common mangrove part used to obtain crude extract as supported by 42.1% of the 59 published studies (Figure 5B).

ANTIMICROBIAL COMPOUNDS IDENTIFIED FROM SOUTHEAST ASIAN MANGROVES

29 species were successful in extraction with diverse elucidated bioactive compounds. Collectively, the Southeast Asian mangroves species possessed 49 bioactive compounds that exhibited antibacterial activity. Moreover, the antibacterial effect constitutes (n=50) 71.4% of the overall antimicrobial activities that mangroves can exhibit with reference to 59 final reviewed studies.

Aside from that, 32 antifungal, 13 antiprotozoal, and 12 antiviral bioactive compounds were also isolated. However, no anthelminthic compounds were reported.

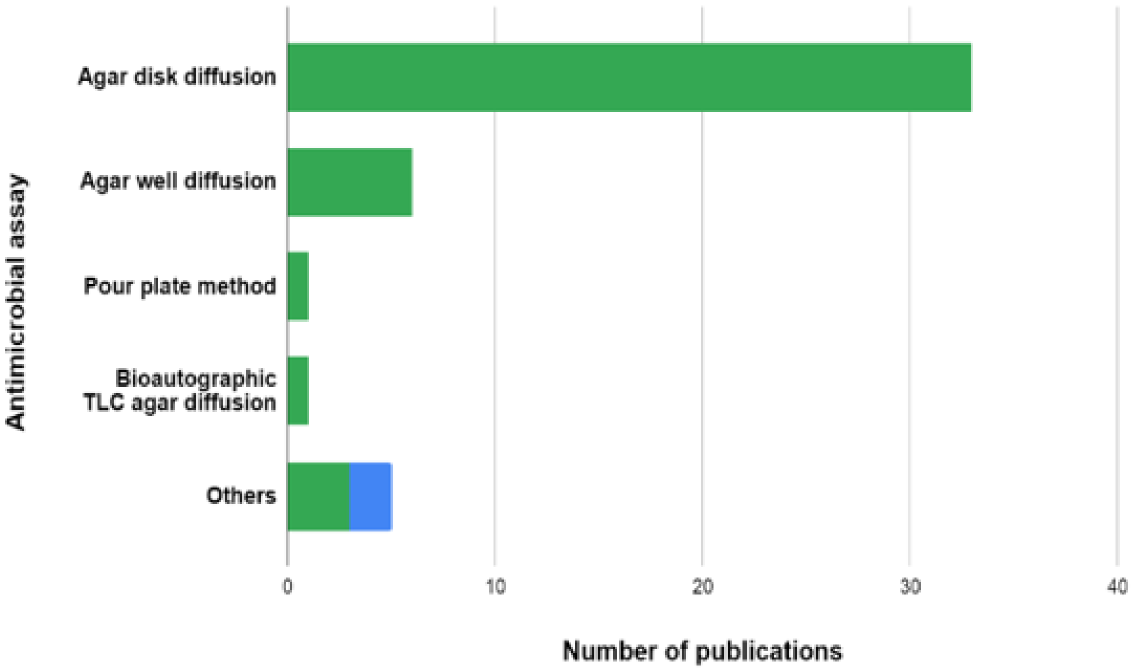


FIGURE 6. Frequency of various antimicrobial susceptibility tests utilized in screening Southeast Asian mangroves in terms of the number of publications. TLC means Thin-Layer Chromatography. The “others” indicate the antiviral (green bar) and antiprotozoal (blue bar) assay

ANTIMICROBIAL ASSAYS APPLIED TO DETERMINE THE ANTIMICROBIAL EFFICACY OF SOUTHEAST ASIAN MANGROVES

The summary data of Southeast Asian mangroves with the resulted zone of inhibition after antimicrobial testing as well as inhibitory concentration values are shown in this review. In terms of antimicrobial screening, Figure 6 demonstrates the well-known antimicrobial assays with the incorporation of antiviral- and antiprotozoal-related tests denoted by "others" in the stacked bar chart. The agar disk diffusion (Kirby-Bauer) method is the most utilized which is supported by 33 studies (71.7%) compare with agar well diffusion (n=6) constituting only 13.0%. This is followed by other methods such as the pour plate method and bioautographic Thin Layer Chromatography (TLC) agar diffusion, both of which were once used. Other methods refer to antiviral assays (n=3) such as cytopathic effect inhibition (CPE), firefly luciferase assay system, and cell culture method. Additionally, one (1) antiprotozoal assay was utilized and identified as DAPI (4',6-diamidino-2-phenylindole) high-throughput anti-malarial assay.

INHIBITORY CONCENTRATION ASSAYS UTILIZED TO FURTHER DETERMINE THE ANTIMICROBIAL EFFICACY OF SOUTHEAST ASIAN MANGROVES

The bar chart in Figure 7 showed the frequency of inhibitory concentration assays applied in the final included studies after antimicrobial susceptibility screening. The figure shows that broth microdilution is the most used since it represents 51.4% (n=37) of the entire inhibitory concentration tests. Moreover, it was followed by agar dilution (n=3) while the least used assay is broth macrodilution. These methods yielded varying minimum inhibitory concentration (MIC) values for various Southeast Asian mangroves. Aside from MIC values, half-maximal inhibitory concentration (IC_{50}) values were also secondarily sought. To completely confirm the antimicrobial effect of mangrove plant extract, the microbicidal ability of mangroves was investigated. Figure 8 revealed the graphical distribution of microbicidal assays in the 59 studies reviewed. It can be deemed that minimum bactericidal concentration (MBC) is the most employed microbicidal assay which is supported by eight (61.5%) published studies. On the other hand, the time-kill test garnered second in terms of highest frequency which represents 23.1% (n=3) in the overall employed microbicidal assays.

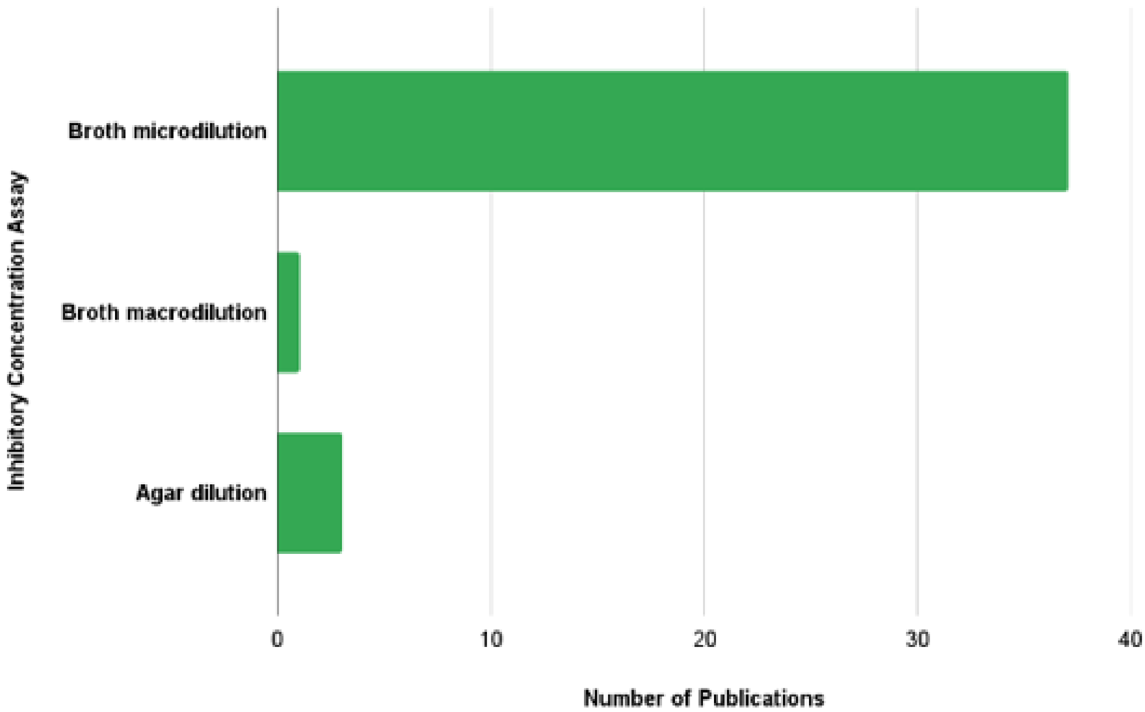


FIGURE 7. Frequency of inhibitory concentration assays by the number of publications. Minimum inhibitory concentration (MIC) tests highlight dilution methods

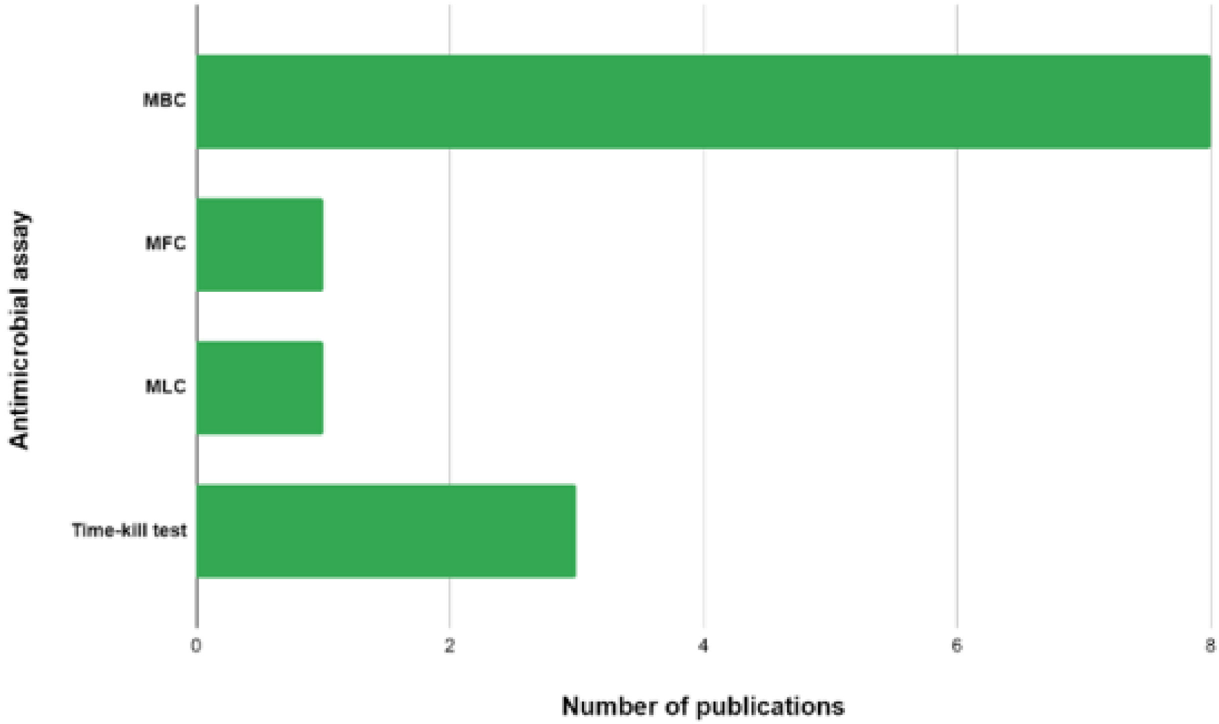


FIGURE 8 Microbicidal assays applied during the antimicrobial screening of mangrove plant extracts which is presented by the number of publications. MBC= Minimum Bactericidal Concentration, MFC= Minimum Fungicidal Concentration, and MLC= Minimum Lethal Concentration.

TABLE 1. Patent claim and information concerning Southeast Asian mangroves

Patent	Inventor	Country	Year	Title	Type of Extract	Company	Claimed
WO2014027958A1	Ho Sup Yoon, Ding Xiang Liu, Quoc Toan Nguyen	Singapore	2014	Anti-viral methods and the use of an anti-viral agent	Protein extraction buffer	Nanyang Technological University	Antiviral

SOUTHEAST ASIAN MANGROVES AND THEIR SYNERGISM WITH DRUGS

One study presented and proved that Southeast Asian mangrove species *M. malabathricum* exhibited synergistic activity with amoxicillin against pathogens. For the synergism with amoxicillin drug, the combination of extract and antibiotic garnered a FICI value of 0.5 synergistic categories against Gram-positive bacteria *Bacillus cereus, Staphylococcus aureus*, as well as Gram-negative bacteria *Escherichia coli* and *Proteus mirabilis* (Apridamayanti et al. 2021).

PATENT REVIEW REGARDING SOUTHEAST ASIAN MANGROVE AS AN ANTIMICROBIAL AGENT

Based on Table 1, a patent was filed last 2014 by Yoon et al. which focuses on the antiviral activity of *Viscum ovalifolium*, a mangrove-associate epiphyte from the Loranthaceae family. It is a Southeast Asian mangrove species from Singapore which contains lectin as an antiviral agent against the dengue virus.

QUALITY ASSESSMENT AND RISK OF BIAS IN STUDIES

In terms of the quality of the 59 included studies, most of them were categorized under medium to high risk of bias. The studies scored poorly due to inconsistent control groups and mangrove extract tested to specific microorganisms only without encompassing other types of microbes. Additionally, all the included studies have various protocols for extraction methods as well as the solvent used. Likewise, they employed different antimicrobial assays for each type of microorganism. Hence, the studies reviewed are quite heterogeneous.

DISCUSSION

In the systematic review of the antimicrobial activities of mangrove species in Southeast Asia, numerous articles were acquired to evaluate the methodological quality and reported antimicrobial efficacy of mangroves extracts. Moreover, existing patents were also obtained to provide an overview of mangrove as an antimicrobial agent for prospective applications in the pharmaceutical industry. Only less than 3% of the overall deduplicated studies and patents passed the stringent criteria needed for them to be included in this review. This result emphasizes the relevance of upholding research in this area and further exploring the horizon of mangroves in the field of applied microbiology and pharmaceuticals. After the study selection using the PRISMA flow diagram, a thorough data extraction process was conducted. Out of 59 in vitro antimicrobial studies, two (2) of them which were published by Sibero et al. (2020) and Sirichoat et al. (2021) did not report positive antimicrobial activity at all. The ineffective activity of mangroves as reported by the mentioned studies highlighted the fact that there may be a specific part of a plant that exhibits the highest inhibitory action against microorganisms.

On the other hand, based on a worldwide standpoint, Southeast Asia supports the biggest area of potentially most species-diverse mangroves (Giesen et al. 2006). In terms of the number of studies per country, 20 articles originated from Indonesia while in Malaysia, there are 19, and in Cambodia, there is only one. Hence, it can be interpreted that when a country has a bigger mangrove area, more studies about mangroves arise. Indonesia holds the greatest area of mangroves with an amount of 4.5 million ha (Honculada-Primavera 2000; Spalding et al. 1997). Furthermore, Laos was supposed to be excluded from this study since according to Yahya et al. (2020), it is the only Southeast Asian country that lacks mangroves due to its geographic characteristic as a landlocked country. Contrastingly, the current systematic review was successful in retrieving an article concerning a mangrove originating from Laos (Prajuabjinda et al. 2012) that tackled the antimicrobial effect of *Hydnophytum formicarum* Jack, an epiphytic mangrove-associate plant. Thus, research regarding mangroves from Laos and other landlocked countries must be upheld.

Several mangrove species are widespread, especially in Southeast Asia. One of those is *Sonneratia alba*, which is a prevalent mangrove species in the Indo-West Pacific region and is extensively scattered from East Africa through Southeast Asia to Southern Japan and Northeastern Australia (Yang et al. 2017). It is also the most studied species in the review. It is an evergreen tree and a true mangrove plant that is best known for its development of aerial roots, which is done to manage the required atmospheric oxygen at the absorbing surfaces (Pratiwi 2021; Spalding 2004). Conversely, Rhizophoraceae is the most studied family. Rhizophoraceae has three unique characteristics—high salt tolerance, aerial roots, and viviparous embryogenesis. Interestingly, its embryo starts germination without dormancy and it grows out of the fruit and the seed coat while still being affixed to the parent plant (Guo et al. 2017).

Mangroves are a diverse group of woody vegetation types that live in brackish and marine environments. There are two types of mangroves which are categorized as true mangroves and mangrove associates. True mangroves are species that live in the coastal habitat only, while mangrove associates are plants that are often found along with the mangroves and are mostly found in landward margins. Mangroves have different plant forms, they can be creepers, ferns, herbs, orchids, palms, shrubs, vines, and trees (Giesen et al. 2006; United Nations Development Programme 2018).

For the mangrove species that have proven to be a potential source of antimicrobial compounds, an extraction method must be performed first. This method is necessary for the separation of bioactive compounds from plant material before testing it for antimicrobial activity. As seen in the extraction methods, maceration is the most used. To support this claim, maceration is one of the traditional and common techniques (Alara et al. 2018; Belwal et al. 2018; Cacique et al. 2020; Ćujić et al. 2016) since it is a low-cost method for isolating biologically active compounds as well as essential oils (Srivastava et al. 2021). Maceration involves pouring a solvent into a container with granulated plant material until entirely covered. Afterward, it should be sealed and kept for at least 72 hours (Abubakar & Haque 2020; Azwanida 2015; Doughari 2012; Ingle et al. 2017; Majekodunmi 2015; Pandey & Tripathi 2014; Ujang et al. 2013).

Subsequently, methanol is a widely used solvent in the extraction process because it can generate greater extraction yields since this organic solvent is characterized by high polarity (Hassim et al. 2014). Additionally, methanol is a good solvent that demonstrated an elevated extraction yield for solid-liquid extraction techniques, for instance, maceration of plant material (Borges et al. 2020). Moreover, several studies reported the effectiveness of exploiting a leaf part upon preparing different extracts (Burman et al. 2018; Yompakdee et al. 2012).

Additionally, the presentation of mangrove species with reported bioactive compounds merely served as supplemental data to corroborate the significance of extraction methods in attesting to the antimicrobial activity of Southeast Asian mangroves. Out of the final 59 included articles, only 28 studies covered the identification of bioactive compounds as one of the objectives of their study. Of the total 28 studies, 20 of them isolated conventional bioactive compounds which are known as phytochemicals and their other derivatives while surprisingly, other studies (n=8) isolated novel compounds. These include a new lupane-type triterpenoid (Harizon et al. 2015); eight thaixylomolins G−N, two phragmalins, and two mexicanolides (Li et al. 2015); hydroxyavicenol C and glycosemiquinone (Mazlan et al. 2020); moluccensins H-J (Pudhom et al. 2010); five thaigranatins A–E (Ren et al. 2018); scataccanol (Suthiwong et al. 2016); 12-hydroxycorniculatolide A (Wongsomboon et al. 2018) and 29 limonoids specifically xylomolins A1–A7, B1–B2, C1–C2, D–F, G1–G5 (Zhang et al. 2018).

In the search for antimicrobial agents for potential pharmaceutical use, in vitro antimicrobial susceptibility screening is primarily performed. In the case of Southeast Asian mangroves, the portion of its extracts has been subjected to various assays to assess its antimicrobial and inhibitory capability against pathogens. Moreover, it reported notable inhibition zone (mm), inhibitory concentration (µg/ml), and microbicidal concentration (µg/ml) values exhibited by mangroves. Furthermore, some mangroves are labeled with no inhibitory effect due to their ineffectiveness against all tested microbial pathogens.

The most employed test to acquire a zone of inhibition is agar disk diffusion which utilizes paper disks saturated with antimicrobial agents and the disks are placed on the agar surface seeded with bacteria. Afterward, the plate is incubated overnight and the presence or absence of a zone of inhibition around the disks is measured (Tenover 2015). This method is mostly used because it is a simple, cost-efficient, and official method used for testing antimicrobial susceptibility. Other methods are not widely applied because they require specific equipment even though they can provide rapid results of the activity or effects of antimicrobial agents (Balouiri et al. 2016).

The more effective way of presenting the antimicrobial activity of plant extract is through further performing MIC tests. Hence, it is included in the eligibility criteria. Minimum inhibitory concentration (MIC) is the gold standard for the determination of the organisms' susceptibility (microbiostatic) to antimicrobials through the lowest concentration (Andrews 2001). The broth microdilution is a rapid, inexpensive, and standard method of defining the MIC quantitatively (Luber et al. 2003; Moreno et al. 2013).

Moreover, it permits a huge quantity of replicates even with a small amount of sample. As opposed to macrodilution, it is easier and more effective in interpreting the inhibitory concentration (Moreno et al. 2013). The best or ideal MIC value is as low as <0.5 mg/mL or 500 µg/mL (Cappelli & Mariani 2021) which can be highly reflected in one of the 59 reviewed studies specifically in the article generated by Prajuabjinda et al. (2012).

Normally, after broth dilution, the minimum bactericidal concentration (MBC) is conducted. It is a standardized antimicrobial susceptibility test that served as secondary screening after broth dilution, through sub-culturing a sample. It provides the bactericidal endpoint or the smallest possible concentration of plant material that could be obtained to kill 99.9% of bacterial pathogens after one day of incubation (Balouiri et al. 2016; Clinical and Laboratory Standards Institute 1998; Parvekar et al. 2020). Utilizing MBC as a supplementary test is beneficial because it offers the bactericidal concentration in contrast to sole bacteriostatic intensity, hence, it is conducive to the major objective of searching for potent antimicrobial agents (Abedon 2011). All these results infer that screening of inhibitory action against bacteria is the primary focus of antimicrobial studies which used Southeast Asian mangroves as a potential biological agent. In addition to that, the ideal methodology for antimicrobial susceptibility assay of mangroves is through the combination of assessing the zone of inhibition with the help of agar diffusion methods, subsequent dilution methods to test its microbiostatic effect with the lowest concentration, and utilizing microbicidal tests to completely confirm its germicidal effect.

Aside from merely utilizing plant extracts in attempting to combat antimicrobial resistance, other researchers investigated the combination of plant extract and existing commercial drugs to test its synergism effect for further enhancement of antimicrobial activity. For the synergism of *M. malabathricum* extract with amoxicillin drug, the combination of the two garnered a Fractional Inhibitory Concentration Index (FICI) value of 0.5 synergistic categories against *E. coli, B. cereus, S. aureus, and P. mirabilis* (Apridamayanti et al. 2021). This means that the combinatorial effect of *M. malabathricum* leaves extract and amoxicillin increases the inhibitory activity, thus, further minimization of MIC may be induced on one or both compounds than on the compounds alone. The synergism of plants with drugs is crucial because it allows the use of lower drug doses of the combination constituents. This would even reduce unfavorable or adverse reactions (Tallarida 2011). The findings regarding the Southeast Asian mangroves and their synergism with drug implies that this area is understudied due to the reason that the PRISMA flow diagram managed to collate only one study with reference to the inclusion criteria. Hence, further pursuits on mangrove plants and drug interaction are highly encouraged.

Before the plant extract with attested antimicrobial activity become an agent viable and adequate for technological (e.g., pharmaceutical industry) use, it may normally proceed first to patent application. Patents are important documents that legally protect invention and it contains information for technological analysis (Clinical and Laboratory Standards Institute 2006; dos Santos et al. 2017). It can also provide a technological overview of the inventions concerning mangrove plant extracts and their antimicrobial activity; wherein this technological overview offers a summary of an idea, method, or invention which is commonly science-based, for industrial application.

In terms of patent review of the antimicrobial activity of Southeast Asian mangroves, there is no available related systematic review up to this date, hence, it is included in the current study as a medium of conveying technological information and invention associated with mangroves. As an outcome, one patent (Yoon et al. 2014) was obtained regarding the antiviral activity of *Viscum ovalifolium* which contains lectin. The protein extraction buffer helped in isolating lectins and it was further subjected to an antiviral test with four serotypes of dengue viruses (DENV). Results showed that it exhibited minimum virus inhibitory effect to all four serotypes due to the blockage that the lectin created on the protein-protein interactions of the viral protein E. Additionally, it lessened viral replication by 25%. This invention may be developed further into therapeutics for dengue. This patent may provide future directions for studies regarding the antimicrobial activity specifically the antiviral action of Southeast Asian mangroves.

Finally, the methodological quality of each included study was assessed by the reviewers based on the formulated 16 parameters that are associated with the extraction and antimicrobial assay methods. Even though most of the studies were identified under medium to high risk of bias, this solely entails a likelihood and level of a specific study to have an occurrence of bias which may lead to less credibility. This risk of bias is primarily based on comparing and assessing each final included study in connection to the aim of this systematic review which was to report antimicrobial activities of mangroves with diverse methods. Hence, the risk of bias can be prevented by conducting and exploring various mangrove parts, extraction methods, solvents, and a wide range of indicator pathogens for antimicrobial assays.

Identifying the risk of bias is vital because it helps the readers to critically and independently study scientific information to prevent inadequate or potentially dangerous treatments (Pannucci & Wilkins 2010). On the other hand, quality assessment is important, especially in a systematic review because it is an indicator of the strength of evidence on where conclusions are based. It also enables comparisons of studies depending on the risk of bias (Whiting et al. 2017).

CONCLUSION

Following the PRISMA protocol, Southeast Asia is deemed to have numerous species-diverse mangroves. Moreover, the predominant extraction method is macerating leaf tissue with methanol. Subsequently, the obtained crude extracts possessed diverse and novel bioactive compounds which can be tapped for antimicrobial efficacy. In the search for antimicrobial agents for potential pharmaceutical use, the in vitro susceptibility screening performed for mangroves were agar disk diffusion, broth microdilution, and minimum bactericidal concentration test. On the other hand, one patent reported a mangrove with proven antiviral efficacy.

Within Southeast Asia, it was observed that as the country contains larger mangrove areas, more antimicrobial studies are published. Hence, more opportunities for studies to be patented and potentially utilized in the pharmaceutical industry to combat antimicrobial resistance. This systematic review may shed light on future perspectives of studies regarding the antimicrobial activities of mangroves which must be continually substantiated in imminent animal and clinical experiments. Furthermore, mangroves from Southeast Asia are anticipated to be a future treatment for infectious diseases.

Protecting and conserving mangroves is essential to ensuring the health and resilience of coastal ecosystems in Southeast Asia, given the rising evidence of the diversity of mangrove species' applications and value in various industries. The development of robust regulatory frameworks, the engagement of local communities, the promotion of sustainable aquaculture, the restoration of degraded mangroves, and the formation of partnerships can guarantee the long-term survival of these critical mangrove species and ecosystems. Countries in Southeast Asia must enact and enforce laws and regulations protecting mangroves and penalize those who harm them. This can include the establishment of protected areas, the regulation of mangrove harvesting and logging, and the establishment of fines for illicit activity. Local people are major partners in the conservation and protection of mangroves, and their participation is crucial to the long-term viability of any conservation project; therefore, local engagement is required. Governments and non-governmental organizations can collaborate with communities to promote knowledge about the significance of mangroves, provide alternate means of subsistence, and involve them in monitoring and restoration activities. Recognizing aquaculture's significance as a primary driver of mangrove degradation in Southeast Asia and supporting sustainable techniques will help mitigate this effect. Restoring degraded mangrove ecosystems can assist in reversing the decline of these essential ecosystems. New mangroves can be planted, invasive species can be eliminated, and water quality can be enhanced through restoration efforts. Collaboration between governments, NGOs, and other stakeholders is essential for the conservation and protection of mangroves. Partnerships can assist leverage resources, facilitate the exchange of knowledge and skills, and promote conservation and restoration best practices. Investing in mangrove protection and restoration can have several positive outcomes, such as mitigating climate change, maintaining biodiversity, and promoting sustainable economic development. As such, it is a crucial component of an all-encompassing strategy for building a more sustainable future.

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REFERENCES

Abed, S. A., Sirat, H. M. & Taher, M. 2013. Total phenolic, antioxidant, antimicrobial activities and toxicity study of *Gynotroches axillaris* Blume (Rhizophoraceae). *EXCLI Journal*. DOI:https://doi.org/10.17877/de290r-10755.

Abedon, S. 2011. Phage therapy pharmacology: Calculating phage dosing. *Advances in Applied Microbiology* 77: 1–40. DOI:https://doi.org/10.1016/b978-0-12-387044-5.00001-7.

Abubakar, A. R. & Haque, M. 2020. Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. *Journal of Pharmacy and Bioallied Sciences* 12(1): 1–10. DOI:https://doi.org/10.4103/jpbs.jpbs_175_19.

Alara, O. R., Abdurahman, N. H., Ukaegbu, C. I. & Azhari, N. H. 2018. *Vernonia cinerea* leaves as the source of phenolic compounds, antioxidants, and anti-diabetic activity using microwave-assisted extraction technique. *Industrial Crops and Products* 122: 533–544. DOI:https://doi.org/10.1016/j.indcrop.2018.06.034.

Alnajar, Z. A. A., Abdulla, M. A., Ali, H. M., Alshawsh, M. A. & Hadi, A. H. A. 2012. Acute toxicity evaluation, antibacterial, antioxidant and immunomodulatory effects of *Melastoma malabathricum*. *Molecules* 17(3): 3547–3559. DOI:https://doi.org/10.3390/molecules17033547.

Alwash, M. S., Ibrahim, N. & Ahmad, W. Y. 2013. Identification and mode of action of antibacterial components from *Melastoma malabathricum* Linn leaves. *American Journal of Infectious Diseases* 9(2): 46–58. DOI:https://doi.org/10.3844/ajidsp.2013.46.58.

Alzabt, A. M. & Rukayadi, Y. 2021. Antibacterial activity of taro (*Colocasia esculenta* (L.) Schott) leaves extract against foodborne pathogens and its effect on microbial population in raw chicken meat. *Food Research* 5(2): 401–409. DOI:https://doi.org/10.26656/fr.2017.5(2).523.

Andrews, J. M. 2001. Determination of minimum inhibitory concentrations. *Journal of Antimicrobial Chemotherapy* 48(1): 5–16. DOI:https://doi.org/10.1093/jac/48.suppl_1.5.

Andriani, D., Revianti, S. & Prananingrum, W. 2020. Identification of compounds isolated from a methanolic extract of *Acanthus ilicifolius* leaves and evaluation of their antifungal and antioxidant activity. *Biodiversitas* 21(6). DOI:https://doi.org/10.13057/biodiv/d210625.

Andriani, Y., Ramli, N. M., Syamsumir, D. F., Kassim, M. N. I., Jaafar, J., Aziz, N. A., ... & Mohamad, H. 2015. Phytochemical analysis, antioxidant, antibacterial and cytotoxicity properties of keys and cores part of *Pandanus tectorius* fruits. *Arabian Journal of Chemistry* 12(8): 3555–3564. DOI:https://doi.org/10.1016/j.arabjc.2015.11.003.

Apridamayanti, P., Sari, R., Rachmaningtyas, A. & Aranthi, V. 2021. Antioxidant, antibacterial activity and FICI (Fractional Inhibitory Concentration Index) of ethanolic extract of *Melastoma malabathricum* leaves with amoxicillin against pathogenic bacteria. *Nusantara Bioscience* 13(2): 140-147. DOI:https://doi.org/10.13057/nusbiosci/n130202.

Azwanida, N. N. 2015. A review on the extraction methods use in medicinal plants, principle, strength

and limitation. *Medicinal & Aromatic Plants* 4(3). DOI:https://doi.org/10.4172/2167-0412.1000196.
Balouiri, M., Sadiki, M. & Ibnsouda, S. K. 2016. Methods for in vitro evaluating antimicrobial activity: A review. *Journal of Pharmaceutical Analysis* 6(2): 71–79. DOI:https://doi.org/10.1016/j.jpha.2015.11.005.
Belwal, T., Ezzat, S. M., Rastrelli, L., Bhatt, I. D., Daglia, M., Baldi, A., ... & Atanasov, A. G. 2018. A critical analysis of extraction techniques used for botanicals: Trends, priorities, industrial uses and optimization strategies. *Trends in Analytical Chemistry* 100: 82–102. DOI:https://doi.org/10.1016/j.trac.2017.12.018.
Borges, A., José, H., Homem, V. & Simões, M. 2020. Comparison of Techniques and Solvents on the Antimicrobial and Antioxidant Potential of Extracts from *Acacia dealbata* and *Olea europaea*. *Antibiotics* 9(2): 48. DOI:https://doi.org/10.3390/antibiotics9020048.
Burman, S., Bhattacharya, K., Mukherjee, D. & Chandra, G. 2018. Antibacterial efficacy of leaf extracts of *Combretum album* Pers. against some pathogenic bacteria. *BMC Complementary and Alternative Medicines* 18(1). DOI:https://doi.org/10.1186/s12906-018-2271-0.
Cacique, A. P., Barbosa, É. S., Pinho, G. P. & de, Silvério, F. O. 2020. Maceration extraction conditions for determining the phenolic compounds and the antioxidant activity of *Catharanthus roseus* (L.) G. Don. *Ciênca e Agrotecnologia* 44. DOI:https://doi.org/10.1590/1413-7054202044017420.
Cappelli, G. & Mariani, F. 2021. A systematic review on the antimicrobial properties of Mediterranean wild edible plants: We still know too little about them, but what we do know makes persistent investigation worthwhile. *Foods* 10(9): 2217. DOI:https://doi.org/10.3390/foods10092217.
Chandra, H., Bishnoi, P., Yadav, A., Patni, B., Mishra, A. P. & Nautiyal, A. R. 2017. Antimicrobial resistance and the alternative resources with special emphasis on plant-based antimicrobials-A review. *Plants* 6(4): 16. DOI:https://doi.org/10.3390/plants6020016.
Chassagne, F., Samarakoon, T., Porras, G., Lyles, J. T., Dettweiler, M., Marquez, L., ... & Quave, C. L. 2021. A systematic review of plants with antibacterial activities: A taxonomic and phylogenetic perspective. *Frontiers in Pharmacology* 11: 586548. DOI:https://doi.org/10.3389/fphar.2020.586548.
Chereau, F., Opatowski, L., Tourdjman, M. & Vong, S. 2017. Risk assessment for antibiotic resistance in South East Asia. *BMJ* 358(Supp. 1): j3393. DOI:https://doi.org/10.1136/bmj.j3393.
Clinical and Laboratory Standards Institute (CLSI). 1998. *Methods for Determining Bactericidal Activity of Antimicrobial Agents*. Approved Guideline, CLSI document M26-A. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA.
Clinical and Laboratory Standards Institute (CLSI). 2006. *Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically* (7th Ed.). Clinical and Laboratory Standards Institute (CLSI).
Cocco, A. R., de Oliveira da Rosa, W. L., da Silva, A. F., Lund, R. G. & Piva, E. 2015. A systematic review about antibacterial monomers used in dental adhesive systems: Current status and further prospects. *Dental Materials* 31(11): 1345–1362. DOI:https://doi.org/10.1016/j.dental.2015.08.155.
Cucikodana, Y., Malahayati, N. & Widowati, T. W. 2019. Phytochemical Content, Antioxidant and Antibacterial Activity of Mangrove (*Avicennia marina*) Leaves Extract. *International Journal of Recent Science Research* 10(7): 33403-33406. DOI:https://doi.org/10.24327/ijrsr.2019.1007.3663.
Ćujić, N., Šavikin, K., Janković, T., Pljevljakušić, D., Zdunić, G. & Ibrić, S. 2016. Optimization of polyphenols extraction from dried chokeberry using maceration as traditional technique. *Food Chemistry* 194: 135–142. DOI:https://doi.org/10.1016/j.foodchem.2015.08.008.
Dao, T. 2013. Biological Activity of Methanolic Extract Derived from *Ipomoea pes-caprae* (L.) Collected in Xuan Thuy National Park. *Journal of Science of HNUE, Chemical and Biological Science* 58(9): 139-145. https://www.researchgate.net/publication/262943517_BIOLOGICAL_ACTIVITY_OF_METHANOLIC_EXTRACT_DERIVED_FROM_Ipomoea_pes-caprae_L_COLLECTED_IN_XUAN_THUY_NATIONAL_PARK.
dos Santos, D. C., Schneider, L. R., da Silva Barboza, A., Diniz Campos, Â. & Lund, R. G. 2017. Systematic review and technological overview of the antimicrobial activity of *Tagetes minuta* and future perspectives. *Journal of Ethnopharmacology* 208: 8–15. DOI:https://doi.org/10.1016/j.jep.2017.06.046.
Doughari, J. H. 2012. Phytochemicals: Extraction methods, basic structures, and mode of action as potential chemotherapeutic agents. *Phytochemicals - A Global Perspective of Their Role in Nutrition and Health*. DOI:https://doi.org/10.5772/26052.
Doydee, P. & Buot, I. E. Jr. 2010. Mangrove habitat restoration and management in Ranong Province, Thailand. *Proceeding of Coastal Zone Asia-Pacific Conference and World Small-Scale Fisheries Congress, Bangkok, Thailand, October 17-22.*
Eldeen, I., Napiah, N. E. M. & Mohamad, H. 2015. Efficacy of three mangrove plants against 5-lipoxygenase, acetylcholinesterase enzymes and five pathogenic bacterial strains. *Life: International Journal of Health and Life-Sciences* 1(1): 24–37. DOI:https://doi.org/10.20319/lijhls.2015.11.2437.

Emelda, A., Arman, Yuliana, D. & Amin, A. 2015. Antimicrobial potency of *Passiflora foetida* linn from South Sulawesi Indonesia against bacteria in vitro. *International Journal of Pharmacy and Technology* 7(3): 9562-9566. https://www.researchgate.net/publication/292518824_Antimicrobial_potency_of_Passiflora_foetida_linn_from_south_Sulawesi_Indonesia_against_bacteria_in_vitro.

Erwin, Anggeraini, D. & Suryani. 2016. Chemical analysis and antibacterial activity of the ethanolic extract of *Stenochlaena palustris*. *Der Pharmacia Lettre* 8(1): 233-236. https://www.semanticscholar.org/paper/Chemical-analysis-and-antibacterial-activity-of-the-Erwin-Anggeraini/7770d68aedca55c4df2337b1e4ae22eacc449c86.

Fahmi, A. 2016. Antioxidant and Antibacterial Activity Tests of Dragon Scales Leaves Crude Methanol Extracts (*Drymoglossum piloselloides* (L.) Presl). *Proceedings The 3rd AISTSSE: Trends in Science and Science Education*. https://scholar.google.co.id/citations?view_op=view_citation&hl=en&user=nay04RAAAAAJ&citation_for_view=nay04RAAAAAJ:UeHWp8X0CEIC.

Food and Agriculture Organization. 2003. *Status and trends in mangrove area extent worldwide*. Forest Resources Assessment Working Paper No. 63, Rome: Forest Resources Division, FAO. Edited by Wilkie M. L. & Fortuna S. http://www.fao.org/docrep/007/j1533e/j1533e00.

Giesen, W., Wulffraat, S., Zieren, M. & Scholten, L. 2006. *Mangrove Guidebook for Southeast Asia*. Food and Agriculture Organization of the United Nations Regional Office For Asia and The Pacific. Bangkok: Rap Publication. https://www.fao.org/documents/card/en/c/d86e6e7e-1f5e-5ac4-942a-39b3b79abe05/.

Guo, W., Wu, H., Zhang, Z., Yang, C., Hu, L., Shi, X., ... & Huang, Y. 2017. Comparative analysis of transcriptomes in Rhizophoraceae provides insights into the origin and adaptive evolution of mangrove plants in intertidal environments. *Frontiers in Plant Science* 8: 795. DOI:https://doi.org/10.3389/fpls.2017.00795.

Haq, I., Hossain, A. B. M. S., Khandaker, M. M., Merican, A. F., Faruq, G., Boyce, A. B. & Azirun, M. S. 2014. Antioxidant and antibacterial activities of different extracts and fractions of a mangrove plant *Sonneratia alba*. *International Journal of Agriculture & Biology* 16: 707-714. https://www.semanticscholar.org/paper/Antioxidant-and-antibacterial-activities-of-and-of-Haq-Hossain/5250fd98df6b1f9be2ffd472090a53f64a13bb7b.

Haq, M., Sani, W., Hossain, A. B. M. S., Taha, R. M. & Monneruzzaman, K. M. 2011. Total phenolic contents, antioxidant and antimicrobial activities of *Bruguiera gymnorrhiza*. *Journal of Medicinal Plants Research* 5(17): 4112–4118. DOI:https://doi.org/10.5897/jmpr.9001250.

Hardiyanti, R., Marpaung, L., Adnyana, I. K. & Simanjuntak, P. 2018. Antioxidant and antibacterial activities of various extracts of duku's mistletoe leaf (*Dendrophthoe pentandra* (l.) Miq) collected from Medan, Indonesia. *Asian Journal of Pharmaceutical and Clinical Research* 11(12): 526. DOI:https://doi.org/10.22159/ajpcr.2018.v11i12.29725.

Hardiyanti, R., Marpaung, L., Adnyana, I. K. & Simanjuntak, P. 2019. Isolation of Quercitrin from *Dendrophthoe pentandra* (L.) miq Leaves and It's Antioxidant and Antibacterial Activities. *Rāsayan Journal of Chemistry* 12(4): 1822–1827. DOI:https://doi.org/10.31788/rjc.2019.1235353.

Harizon, Pujiastuti, B., Kurnia, D., Sumiarsa, D., Shiono, Y. & Supratman, U. 2015. Antibacterial triterpenoids from the bark of *Sonneratia alba* (Lythraceae). *Natural Product Communications* 10(2): 277–280. DOI:https://doi.org/10.1177/1934578x1501000215.

Hassim, N., Markom, M., Anuar, N. & Baharum, S. N. 2014. Solvent selection in extraction of essential oil and bioactive compounds from *Polygonum minus*. *Journal of Applied Sciences* 14(13): 1440–1444. DOI:https://doi.org/10.3923/jas.2014.1440.1444.

Hlashwayo, D. F., Barbosa, F., Langa, S., Sigaúque, B. & Bila, C. G. 2020. A systematic review of in vitro activity of medicinal plants from Sub-Saharan Africa against *Campylobacter* spp. *Evidence-Based Complementary and Alternative Medicine*. 1-13. DOI:https://doi.org/10.1155/2020/9485364.

Honculada-Primavera, J. 2000. Mangroves of Southeast Asia. *Mangrove-Friendly Aquaculture: Proceedings of the Workshop on Mangrove-Friendly Aquaculture organized by the SEAFDEC Aquaculture Department, January 11-15, 1999, Iloilo City, Philippines* 1-12. Edited by Primavera, J. H., Garcia, L. Ma. B., Castaños, M. T. & Surtida, M. B. http://hdl.handle.net/1086r2/1947.

Ingle, K. P., Deshmukh, A. G., Padole, D. A., Dudhare, M. S., Moharil, M. P. & Khelurkar, V. C. 2017. Phytochemicals: Extraction methods, identification and detection of bioactive compounds from plant extracts. *Journal of Pharmacognosy and Phytochemistry* 6(1): 32-36. https://www.phytojournal.com/archives/2017/vol6issue1/PartA/6-1-23-924.pdf.

Kaewpiboon, C., Lirdprapamongkol, K., Srisomsap, C., Winayanuwattikun, P., Yongvanich, T., Puwaprisirisan, P., … & Assavalapsakul, W. 2012. Studies of the in vitro cytotoxic, antioxidant, lipase inhibitory and antimicrobial activities of selected Thai medicinal plants. *BMC Complementary and Alternative Medicine* 12(1): 217. DOI:https://doi.org/10.1186/1472-6882-12-217.

Khumaidah, L., Purnomo, A. S. & Fatmawati, S. 2019. Antimicrobial activity of *Sonneratia ovata* Backer. *HAYATI Journal of Biosciences* 26(4): 152-155.

DOI:https://doi.org/10.4308/hjb.26.4.152.
Kudera, T., Fiserova, B., Korytakova, M., Doskocil, I., Salmonova, H., Tulin, E. E., … & Kokoska, L. 2021. In vitro selective antibacterial and antiproliferative effects of ethanolic extracts from Cambodian and Philippine plants used in folk medicine for diarrhea treatment. *Frontiers in Pharmacology* 12: 746808. DOI:https://doi.org/10.3389/fphar.2021.746808.
Li, W., Jiang, Z., Shen, L., Pedpradab, P., Bruhn, T., Wu, J. & Bringmann, G. 2015. Antiviral limonoids including khayanolides from the Trang mangrove plant *Xylocarpus moluccensis*. *Journal of Natural Products* 78(7): 1570–1578. DOI:https://doi.org/10.1021/acs.jnatprod.5b00151.
Lillo, E. P. & Buot, I. E. Jr. 2016. Species Composition of Argao Mangrove Forest, Cebu, Philippines. *Journal of Wetlands Biodiversity* 6. https://www.muzeulbrailei.ro/images/naturale/Volum%20 6/04JWB201663745.pdf.
Luber, P., Bartelt, E., Genschow, E., Wagner, J., & Hahn, H. 2003. Comparison of broth microdilution, E Test, and agar dilution methods for antibiotic susceptibility testing of *Campylobacter jejuni* and *Campylobacter coli*. *Journal of Clinical Microbiology* 41(3): 1062–1068. DOI:https://doi.org/10.1128/jcm.41.3.1062-1068.2003.
Majekodunmi, S. O. 2015. Review of Extraction of Medicinal Plants for Pharmaceutical Research. *Merit Research Journal of Medicine and Medical Sciences* 3(11): 521–527. https://meritresearchjournals.org/mms/content/2015/November/Majekodunmi.pdf.
Mangroves Field Identification Manual of Timor Leste. 2018. *United Nations Development Program-National Directorate of Forestry, Coffee and Industrial Plants, Ministry of Agriculture and Fisheries of Democratic Republic of Timor-Leste*. https://www.tl.undp.org/content/timor_leste/en/home/library/resilience/mangroves-field-identification-manual-of-timor-leste-.html.
Mar, T. Y., Win, H. H. & Yee, M. M. 2020. Antimicrobial, Anti-diabetic and Antioxidant Activities of the Leaf of *Morinda citrifolia* Linn. *University Journal of Creativity and Innovative Research* 1(1). https://www.semanticscholar.org/paper/Antimicrobial%2C-Anti-diabetic-and-Antioxidant-oftheLinnYu/ed8e9657194650aad63af17598970bbdcafe373d.
Mazlan, N. W., Clements, C. & Edrada-Ebel, R. 2020. Targeted isolation of anti-trypanosomal naphthofuran-quinone compounds from the mangrove plant *Avicennia lanata*. *Marine Drugs* 18(12): 661. DOI:https://doi.org/10.3390/md18120661.
Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G. & PRISMA Group. 2009. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Annals of Internal Medicine* 151(4): 264–269. DOI:https://doi.org/10.7326/0003-4819-151-4-200908180-00135.
Moreno, P. R. H., da Costa-Issa, F. I., Rajca-Ferreira, A. K., Pereira, M. A. A. & Kaneko, T. M. 2013. Native Brazilian plants against nosocomial infections: A critical review on their potential and the antimicrobial methodology. Cu*rrent Topics in Medicinal Chemistry* 13: 3040–3078. DOI:https://doi.org/10.2174/15680266113136660219.
Muangrom, W. & Vajrodaya, S. 2018. Comparative phytochemistry and antibacterial properties of *Guettarda speciosa* L. *Kasetsart University Knowledge Repository*. https://kukr2.lib.ku.ac.th/kukr_es/BKN_SCI/search_detail/dowload_digital_file/382786/109212.
Musdja, M. Y., Aeni, M. & Djajanegara I. 2018. Comparison of antibacterial activities leaves extracts of *Cerbera manghas* and leaves extracts of *Azadirachta indica* against *Klebsiella pneumoniae*. *Asian Journal of Pharmaceutical and Clinical Research* 11(3): 51. DOI:https://doi.org/10.22159/ajpcr.2018.v11s3.30030.
Musdja, M. Y., Chadidjah & Djajanegara, I. 2019. Antibacterial activity of dichloromethane and ethyl acetate extracts of bintaro leaf (*Cerbera manghas*, linn) against *Staphylococcus aureus* and *Escherichia coli*. *International Journal of Current Research* 11(1): 398-402. DOI:https://doi.org/10.24941/ijcr.33901.01.20199.
Mutmainnah, B. Q., Baktir, A. & Ni'matuzahroh. 2020. Characteristics of Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Methicillin Sensitive *Staphylococcus aureus* (MSSA) and their inhibitory response by ethanol extract of *Abrus precatorius*. *Biodiversitas* 21(9): 4076-4085. DOI:https://doi.org/10.13057/biodiv/d210919.
Ngo, L. H., Nguyen, T. H. Y., Tran V. K., Doan, V. V., Nguyen M. V. & Bui, H. T. 2021. Screening antibacterial activity of Vietnamese plant extracts against human pathogenic bacteria. *Asian Journal of Pharmaceutical and Clinical Research* 14(6); 62–65. DOI:https://doi.org/10.22159/ajpcr.2021.v14i6.39790.
Nguyen, Q. & Eun, J. 2013. Antimicrobial activity of some Vietnamese medicinal plants extracts. *Journal of Medicinal Plants Research* 7(35): 2597-2605. DOI:https://doi.org/10.5897/jmpr2013.4452.
Nguyen, T. V. & Nguyen, H. T. 2019. Study on antibacterial effects of several Vietnamese medicine plants and their relationships with polyphenol contents. *Asian Journal of Pharmaceutical and Clinical Research* 12(4): 257–265. DOI:https://doi.org/10.22159/ajpcr.2019.v12i4.32290.
Nugraha, A. S., Permatasari, A. E. N., Kadarwenny, C. P., Pratoko, D. K., Triatmoko, B., Rosyidi, V. A., … & Wangchuk, P. 2020. Phytochemical screening and the antimicrobial and antioxidant activities of medicinal plants of Meru betiri National Park – Indonesia. *Journal of Herbs, Spices & Medicinal Plants* 26(3):

303–314. DOI:https://doi.org/10.1080/10496475.2020.1734136.

Nugraha, A. S., Purnomo, Y. D., Widhi Pratama, A. N., Triatmoko, B., Hendra, R., Wongso, H., … & Keller, P. A. 2022. Isolation of Antimalarial Agents From Indonesian Medicinal Plants: *Swietenia mahagoni* and *Pluchea indica*. *Natural Product Communications* 17(1): 1-5. DOI:https://doi.org/10.1177/1934578x211068926.

O'Neill, J. 2016. Tackling drug-resistant infections globally: Final report and recommendations. *Government of the United Kingdom*. https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf.

Omar, S. N. C., Abdullah, J. O., Khairoji, K. A., Chin, S. C. & Hamid, M. 2012. Potentials of *Melastoma malabathricum* Linn. Flower and fruit extracts as antimicrobial infusions. *American Journal of Plant Sciences* 3(8): 1127–1134. DOI:https://doi.org/10.4236/ajps.2012.38136.

Padzil, K. N. M., Ayob, N. M., Alzabt, A. M. & Rukayadi Y. 2021. Antibacterial activity of taro (*Colocasia esculenta* L.) leaves extracts against *Staphylococcus aureus* and *Vibrio parahaemolyticus* and its effect on microbial population in sardine (*Sardinella longiceps* Val.). *Food Research* 5: 88–97. DOI:https://doi.org/10.26656/fr.2017.5(2).431.

Pandey, A. & Tripathi, S. 2014. Concept of standardization, extraction and pre phytochemical screening strategies for herbal drug. *Journal of Pharmacognosy and Phytochemistry* 2(5): 115-119. https://www.phytojournal.com/vol2Issue5/Issue_jan_2014/11.pdf.

Pannucci, C. J. & Wilkins, E. G. 2010. Identifying and avoiding bias in research. *Plastic and Reconstructive Surgery* 126(2): 619–625. DOI:https://doi.org/10.1097/prs.0b013e3181de24bc.

Parvekar, P., Palaskar, J., Metgud, S., Maria, R. & Dutta, S. 2020. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of silver nanoparticles against *Staphylococcus aureus*. *Biomaterial Investigations in Dentistry* 7(1): 105–109. DOI:https://doi.org/10.1080/26415275.2020.1796674.

Patra, J. K. & Thatoi, H. N. 2011. Metabolic diversity and bioactivity screening of mangrove plants: a review. *Acta Physiologiae Plantarum* 33(4): 1051–1061. DOI:https://doi.org/10.1007/s11738-010-0667-7.

Prajuabjinda, O., Panthong, S. & Itharat, A. 2012. Antimicrobial activity of Thai medicinal preparation of Khampramong Temple used for cancer treatment and its plant components. *Journal of the Medical Association of Thailand* 95(1): 159-165. https://pubmed.ncbi.nlm.nih.gov/23964460/.

Pratiwi, D. Y. 2021. Antimicrobial Potential of *Sonneratia alba* and *Sonneratia caseolaris* against Shrimp Pathogens. *Asian Journal of Fisheries and Aquatic Research* 12(4): 7–14. DOI:https://doi.org/10.9734/ajfar/2021/v12i430239.

Pratoomsoot, C., Wongkattiya, N. & Sanguansermsri, D. 2020. Synergistic Antimicrobial and Antioxidant Properties of *Coccinia grandis* (L.) Voigt, *Clerodendrum inerme* (L.) Gaertn. and *Acanthus ebracteatus* Vahl. Extracts and Their Potential as a Treatment for Xerosis Cutis. *Complementary Medicine Research* 27(6): 410–420. DOI:https://doi.org/10.1159/000507606.

Pudhom, K., Sommit, D., Nuclear, P., Ngamrojanavanich, N. & Petsom, A. 2010. Moluccensins H-J, 30-ketophragmalin limonoids from *Xylocarpus moluccensis*. *Journal of Natural Products* 73(2): 263–266. DOI:https://doi.org/10.1021/np900583h.

Ren, J.-L., Zou, X.-P., Li, W.-S., Shen, L. & Wu, J. 2018. Limonoids containing a C_1−O−C29 moiety: Isolation, structural modification, and antiviral activity. *Marine Drugs* 16(11): 434. DOI:https://doi.org/10.3390/md16110434.

Ropisah, M., Wan Nur Aqilah, W. M. S., Nurul Haziqah, Y., Alsya Haneeza, M. S., Mohd Syafid, A., Sheikh Ahmad Izaddin, S. M. G. & Shanthi, A. 2020. Phytochemical Analysis and Biological Activities of *Melastoma malabathricum* and *Dissochaeta gracilis*. *Academy of Sciences Malaysia Science Journal* 13(6): 1-6. https://www.akademisains.gov.my/asmsj/article/phytochemical-analysis-and-biological-activities/.

Rosyidah, K., Sari, L. A. P. & Rohman, T. 2020. Investigation on the antibacterial activity of the methanol extract of purun tikus root (*Eleocharis dulcis*). *IOP Conference Series: Materials Science and Engineering* 980: 012039. DOI:https://doi.org/10.1088/1757-899x/980/1/012039.

Saad, S., Taher, M., Susanti, D., Qaralleh, H. & Awang, A. F. I. B. T. 2012. In vitro antimicrobial activity of mangrove plant *Sonneratia alba*. *Asian Pacific Journal of Tropical Biomedicine* 2(6): 427–429. DOI:https://doi.org/10.1016/S2221-1691(12)60069-0.

Saad, S., Taher, M., Susanti, D., Qaralleh, H. & Rahim, N. A. B. A. 2011. Antimicrobial activity of mangrove plant (*Lumnitzera littorea*). *Asian Pacific Journal of Tropical Medicine* 4(7): 523–525. DOI:https://doi.org/10.1016/s1995-7645(11)60138-7.

Saad., S. B., Bakhtiar, M. T., Darnis, D. S., Qaralleh, H., Noorhaidi, N. & Awang, A. F. 2013. Antimicrobial activity of mangrove plant *Acrostichum speciosum*. *Journal of Pure and Applied Microbiology* 7: 253-257. https://www.semanticscholar.org/paper/Antimicrobial-activity-of-mangrove-plant-Saad-Bakhtiar/5690c8fc8275664c56415d4eec2109ef5439de35.

Saptiani, G., Asikin, A. N., Ardhani, F. & Hardi, E. H. 2018. Mangrove plants species from Delta Mahakam, Indonesia with antimicrobial potency. *Biodiversitas* 19(2): 466–471. DOI:https://doi.org/10.13057/

biodiv/d190220.
Sibero, M. T., Sabdono, A., Pribadi, R., Frederick, E. H., Wijaya, A. P., Haryanti, D., … & Igarashi, Y. 2020. Study of biomedical properties of *Rhizophora mucronata* fruit from Rembang, Central Java. I*OP Conference Series: Earth and Environmental Science* 584: 012001. DOI:https://doi.org/1088/1755-1315/584/1/012001.
Sirichoat, A., Kham-Ngam, I., Kaewprasert, O., Ananta, P., Wisetsai, A., Lekphrom, R. & Faksri, K. 2021. Assessment of antimycobacterial activities of pure compounds extracted from Thai medicinal plants against clarithromycin-resistant *Mycobacterium abscessus*. *PeerJ* 9: e12391. DOI:https://doi.org/10.7717/peerj.12391.
Smith, R. L. & Smith, T. M. 2004. *Elements of ecology*. Pearson Education, Benjamin Cummings. San Francisco.
Somchit, M., Hassan, H., Zuraini, A., Chong, L. C., Mohamed, Z. & Zakaria, Z. A. 2011. In vitro anti-fungal and anti-bacterial activity of *Drymoglossum piloselloides* L. Presl. against several fungi responsible for Athlete's foot and common pathogenic bacteria. *African Journal of Microbiology Research* 5(21): 3537-3541. https://www.semanticscholar.org/paper/In-vitro-anti-fungal-and-anti-bacterial-activity-of-Somchit-Hassan/b39a95d1d2d94b4c774c4a53195a9e1f2c8a8558.
Spalding, M., Blasco, F. & Field, C. 1997. *World Mangrove Atlas*. Environmental Unit. http://www.environmentalunit.com/Documentation/04%20Resources%20at%20Risk/World%20mangrove%20atlas.pdf.
Spalding, M. 2004. TROPICAL ECOSYSTEMS | Mangroves. Encyclopedia of Forest Sciences, *Elsevier* 1704–1712.
Srivastava, N., Singh, A., Kumari, P., Nishad, J. H., Gautam, V. S., Yadav, M. … & Kharwar, R. N. 2021. Advances in extraction technologies: isolation and purification of bioactive compounds from biological materials. *Natural Bioactive Compounds* 409–433. DOI:https://doi.org/10.1016/b978-0-12-820655-00021-5.
Sumardi, Basyuni, M. & Wati, R. 2018. Antimicrobial activity of polyisoprenoids of sixteen mangrove species from North Sumatra, Indonesia. *Biodiversitas* 19(4): 1243–1248. DOI:https://doi.org/10.13057/biodiv/d190409.
Sumathy, V., Jothy Lachumy, S., Zuraini, Z. & Sasidharan, S. 2010. Effects of *Stenochlaena palustris* Leaf Extract on Growth and Morphogenesis of Food Borne Pathogen, *Aspergillus niger*. *Malaysian Journal of Nutrition* 16(3): 439–446. https://pubmed.ncbi.nlm.nih.gov/22691997/.
Suthiwong, J., Thongsri, Y. & Yenjai, C. 2016. A new furanocoumarin from the fruits of *Scaevola taccada* and antifungal activity against *Pythium insidiosum*. *Natural Product Research* 31(4): 453–459. DOI:https://doi.org/10.1080/14786419.2016.1188100.
Tallarida, R. J. 2011. Quantitative methods for assessing drug synergism. *Genes & Cancer*. 2(11): 1003–1008. DOI:https://doi.org/10.1177/1947601912440575.
Tan, W.-N., Shahbudin, F. N., Mohamed Kamal, N. N. S. N., Tong, W.-Y., Leong, C.-R. & Lim, J.-W. 2019. Volatile Constituents of the Leaf Essential Oil of *Crinum asiaticum* and their Antimicrobial and Cytotoxic Activities. *Journal of Essential Oil-Bearing Plants* 22(4): 947–954. DOI:https://doi.org/10.1080/0972060x.2019.1683079.
Tenover, F. C. 2015. Antimicrobial Susceptibility Testing☆. *Reference Module in Biomedical Sciences*. DOI:https://doi.org/10.1016/b978-0-12-801238-3.-02486-7.
Thuoc, D. V., Mai, N. N., Ha, L. T., Hung, L. D., Tra, D. H., Hung, N. T. & Hưng, N, P. 2018. Evaluation of Antibacterial, Antioxidant and Antiobese Activities of the Fruit Juice of Crabapple Mangrove *Sonneratia caseolaris* (Linn.). *International Journal of Agricultural Sciences and Natural Resources* 5(2): 25-29. https://www.semanticscholar.org/paper/Evaluation-of-Antibacterial-%2C-Antioxidant-and-of-of-Thuoc-Mai/16abf1ca378932aa3019d0f26c9974a16880419e.
Ujang, Z. B., Subramaniam, T., Diah, M. M., Wahid, H. B., Abdullah, B. B., Rashid, A. H. B. A. & Appleton, D. 2013. Bioguided fractionation and purification of natural bioactives obtained from *Alpinia conchigera* water extract with melanin inhibition activity. *Journal of Biomaterials and Nanobiotechnology* 4(3): 265–272. DOI:https://doi.org/10.4236/jbnb.2013.43033.
Valiela, I., Bowen, J. L., York, J. K. 2001. Mangrove forests: One of the world's threatened major tropical environments. *Bioscience* 51(10): 807. DOI:https://doi.org/10.1641/0006-3568(2001)051[0807:mfootw]2.0.co;2.
Vu, T. T., Kim, H., Tran, V. K., Le Dang, Q., Nguyen, H. T., Kim, H., ... & Kim, J.-C.. 2016. In vitro antibacterial activity of selected medicinal plants traditionally used in Vietnam against human pathogenic bacteria. *BMC Complementary and Alternative Medicine* 16(1). DOI:https://doi.org/10.1186/s12906-016-1007-2.

Wahyuni, T. S., Tumewu, L., Permanasari, A. A., Apriani, E., Adianti, M., Rahman, A., … & Hotta, H. 2013. Antiviral activities of Indonesian medicinal plants in the East Java region against hepatitis C virus. *Virology Journal* 10(1): 259. DOI:https://doi.org/10.1186/1743-422x-10-259.

Whiting, P., Wolff, R., Mallett, S., Simera, I. & Savović, J. 2017. A proposed framework for developing quality assessment tools. *Systematic Reviews* 6(1): 204. https://doi.org/10.1186/s13643-017-0604-6.

Wongsomboon, P., Maneerat, W., Pyne, S. G., Vittaya, L. & Limtharakul née Ritthiwigrom, T. 2018. 12-Hydroxycorniculatolide A from the Mangrove Tree, *Lumnitzera littorea*. *Natural Product Communications* 13(10): 1327-1328. DOI:https://doi.org/10.1177/1934578x1801301023.

Yahya, N., Idris, I., Rosli, N. S. & Bachok, Z. 2020. Mangrove-associated bivalves in Southeast Asia: A review. *Regional Studies in Marine Science* 38: 101382. DOI:https://doi.org/10.1016/j.rsma.2020.101382.

Yang, Y., Li, J., Yang, S., Li, X., Fang, L., Zhong, C., ... & Shi, S. 2017. Effects of Pleistocene sea-level fluctuations on mangrove population dynamics: A lesson from *Sonneratia alba*. *BMC Evolutionary Biology* 17(1): 22. DOI:https://doi.org/10.1186/s12862-016-0849-z.

Yompakdee, C., Thunyaharn, S. & Phaechamud, T. 2012. Bactericidal activity of methanol extracts of Crabapple mangrove tree (*Sonneratia caseolaris* Linn.) against multi-drug resistant pathogens. *Indian Journal of Pharmaceutical Sciences* 74(3): 230–236. DOI:https://doi.org/10.4103/0250-474X.106065.

Yoon, H. S., Liu, D. X. & Nguyen, Q. T. 2014. Anti-viral methods and the use of an anti-viral agent. Singapore Patent. WO2014027958A1.

Zhang, J., Li, W., Dai, Y., Shen, L. & Wu, J. 2018. Twenty-nine new limonoids with skeletal diversity from the mangrove plant, *Xylocarpus moluccensis*. *Marine Drugs* 16(1): 38. DOI:https://doi.org/10.3390/md16010038.

Zuraini, Z., Sasidharan, S., Roopin Kaur, S. & Nithiyayini, M. 2010. Antimicrobial and Antifungal Activities of Local Edible Fern *Stenochlaena palustris* (Burm. F.) Bedd. *Pharmacology Online* 1: 233-237. https://www.semanticscholar.org/paper/Antimicrobial-and-Antifungal-Activities-of-Local-Zuraini-Sasidharan/7399503cb26095c25e00789eb870cfd06b08bd5a

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