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Phytochemical Screening of Mahogany (*Swietenia mahogany*) Secondary Extract Potential as COVID-19 Medication

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Abstract. *Mahogany secondary metabolite is proven effective as lung disease medication, including COVID-19 through docking analysis. Therefore, this study aimed to identify total secondary metabolite from leaves, stem barks, and seeds of mahogany (Swietenia mahogany). The study was carried out using an experimental and descriptive method by observing the visual changes in the sample including color and foam formation, total levels of flavonoids, alkaloids, and saponins using Gas Chromatography and Mass Spectroscopy (GC-MS). Phytochemical analysis was analyzed to identify secondary metabolites namely flavonoids, alkaloids, tannins, triterpenoid saponins, and steroids. The results of the GC-MS analysis showed that mahogany seeds extract had the highest retention time, with a total of 46,484, containing alpha -D Glucopyranoside, 3-Penten-2-one, and gamma-Tocopherol. These compounds belonged to derivatives of flavonoids and saponins, serving as potential COVID-19 medication. The other were terpenoid, steroid, and fatty acid group compounds (alpha humulene, neophyte diene, n-hexadecanoic acid, 9- Octadecenoic acid, Octadecanoic acid, Squalene, and Stigmasterol). In conclusion, these identified compounds have the potential for COVID-19 medication due to their anti-inflammatory, antiviral, antimicrobial immunosuppressant, anticancer, and anti-asthma properties.*

Keywords: *Gas Chromatography; Mass Spectroscopy; Secondary metabolites; Swietenia Mahogany.*

Type of the Paper: Regular Article.

1. Introduction

The world was shocked by a pneumonia outbreak of unknown cause, at the end of 2019. Officially, the World Health Organization (WHO) named this disease as COVID-19 infected by the virus called SARS-CoV-2 (severe acute respiratory syndrome- coronavirus-2) [1]. Based on the study by House et al. [2], the agent of COVID-19 originated from the beta coronavirus genus which belongs to the same genus as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). The virus can pass through mucous membranes, particularly the nasal and laryngeal mucosa, enter the lungs by the respiratory tract, and target organs [3]. After acute-phase management and the patient is cured, the clinicians are currently facing long-term complications, including a large variety of symptoms, defined as “post-acute COVID-19 syndrome” [4]. Radiographic examination exploiting chest x-ray images (CXI) shows there are pulmonary disorders, particularly chronic pulmonary disease [5]. In post-acute COVID-19, some patients develop fibrotic lung disease, such as post-COVID-19 lung disease (PCLD) [6].

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In Indonesia, vaccination has been proven as an effective way to control COVID-19. Based on the 2548 global studies, vaccine administration was suggested to be effective reducer of long-COVID-19 risk or odds with preliminary evidence of one or two doses [7]. The Indonesian government considers the implementation of vaccine urgent to prevent supplies and revive the economy, thereby facilitating quick recovery from virus outbreak [8].

The type of vaccine that currently exists is a viral vector-based, which uses safe viruses to deliver certain proteins to the desired pathogen, thereby triggering the body's immune response without causing disease. Several studies reported that the observed effectiveness of the Pfizer-BioNTech vaccine was 91.2%, the Moderna was 98.1%, while the effectiveness of the CoronaVac was 65.7% [9].

Studies have been conducted on interaction of COVID-19 spike protein with several secondary metabolite compounds, including flavonoids, alkaloids, and saponins in mahogany. The results show that metabolite compounds can interact with the spike protein at the S1 and S2 region [10]. This study bioinformatically confirmed that extract from mahogany could have the potential to overcome the problem of the body's immunity to COVID-19 infection. During the experiment, 35 secondary metabolite plants were selected and docked into the active site of 6LU7 through molecular docking to determine potential inhibitory compounds capable of inhibiting COVID-19 infection pathway. The results showed that *pycnamine* should be examined in vitro to combat COVID-19 [11]. Other secondary metabolic substances that can potentially be developed into vaccine to suppress the spread include flavonoids, alkaloids, and saponins [12]. Therefore, this study aimed to identify secondary metabolites from seeds, stem barks, and leaves of mahogany using the GC-MS method.

2. Materials and methods

2.1. Sample Collection

The sample used in this study was collected from leaves, stem barks, and seeds from *Swietenia mahogany* located in Jl. PBSI Medan Estate. Due to the presence of secondary metabolite, collection was performed only from mahogany without considering age and other factors. The sample collected was stored in the freezer at -20^{o}C and soaked using Ethanol 96% for the macerations process. All part of the sample was sterilized by following three steps namely, cleaning, drying, and grinding. The tools used were Gas Chromatography and Mass Spectroscopy apparatus (GCMS), Glass jars, Rotary evaporator, Buchner funnel, Reaction tubes (Iwaki), Mesh sieve 60, and Filter paper.

2.2. Extraction process

The minimum weight of all sample parts was achieved for analysis of 100 g before soaking in methanol. Subsequently, the extraction method was conducted by following several procedural

steps. These include soaking of sample in methanol for 3 days (3 x 24 hours) at room temperature thereby avoiding light. The filtrate from every sample was collected and concentrated using rotary evaporator until a solution was evaporated [13]. This extraction process was conducted in the Chemical Laboratory, Sumatera Utara University, Medan.

2.3. Phytochemical Screening

Several secondary metabolites were analyzed using certain reagents and procedures. Specifically, flavonoids, alkaloids, and saponins were detected using the method described by Sangi et al. [14].

2.4. GC-MS Analysis

Concentrated extract from leaves, stem barks, and seeds of mahogany were analyzed using GC-MS by injecting into inlet of GC machine. This was followed by filtrate analysis using MS machine. Ion detector was used to calculate the *Total Respond Chromatogram* (TRC) and MS machine showed specific results on peat time or TRC peak.

3. Results and Discussion

The samples used were leaves, stem barks, and seeds of mahogany plants taken and collected from the experimental field at Medan Area University. As shown in Fig. 1, samples were dried and chopped into smaller pieces.

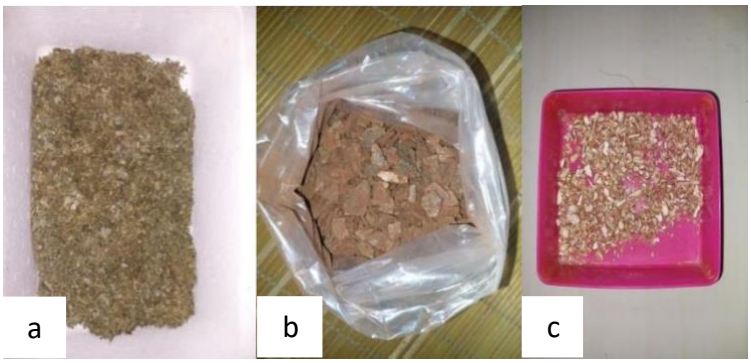

Fig. 1. Grounded sample visualization. a) Dry leaf, b) stem barks, c) seeds

The weight of the dried sample obtained was 200 grams, with variations in water content affecting the maceration process. The lower water content facilitated the process of withdrawing active compounds from the sample. This occurred because the solvent could easily penetrate the cell walls without any interference from water molecules.

3.1. Sample Extraction

The extraction process was carried out using the maceration method to extract the active compounds contained in the sample. The maceration method was conducted to obtain derivatives of active compounds through soaking without heating. This was applied to avoid damage to compound components that were unstable and could not resist heat. The selection of solvent for the maceration method would provide high effectiveness for the extraction efficiency of

polyphenol from *Serpylli herba.* The process was carried out using various extraction methods based on chemical component of the extracted sample, including maceration, heat-assisted extraction, and ultrasonic-assisted extraction [15]. The maceration process for each sample was carried out for 24 hours in a closed room and protected from light. The process of separating the filtrate to be concentrated was performed using *rotary evaporator* to separate extract from the solvent. Subsequently, the results of sample extraction were observed, as presented in Fig. 1.

Table 1. Visualization of sample extract description

Picture	Visual Description
 Leaf extract	• Appear to be black • Typical strong scent • Moderate particle
 Seeds extract	• Appear to be reddish • Typical scent of ground nuts • Little oily • Dense and soft texture
 Stem barks	• Appear to be brownish red • Little scent of ground nuts • Dense and soft texture

3.2. Phytochemical identification from Mahogany

The screening for phytochemical compounds in mahogany extract showed different positive results for each fraction. The results showed that extract contained flavonoids, terpenoids, steroids, tannins, and saponins. Phytochemical test was also conducted to confirm the observations from the GC-MS identification shown in Table 1. However, this study focused on flavonoids, alkaloids, and saponins due to the interaction of COVID-19 spike protein with several mahogany secondary metabolite compounds. Phytochemical screening of mahogany is shown in Table 2.

Secondary flavonoids, alkaloids, and saponins can interact with COVID-19 spike protein

[10]. According to GC-MS analysis and phytochemical screening, flavonoids were not found in mahogany seeds. Therefore, there was an error in interpreting the color of the experimental results. This occurred due to the weakness of the color reaction, leading to difficulty in distinguishing and interpreting when there are two compounds in one test [16].

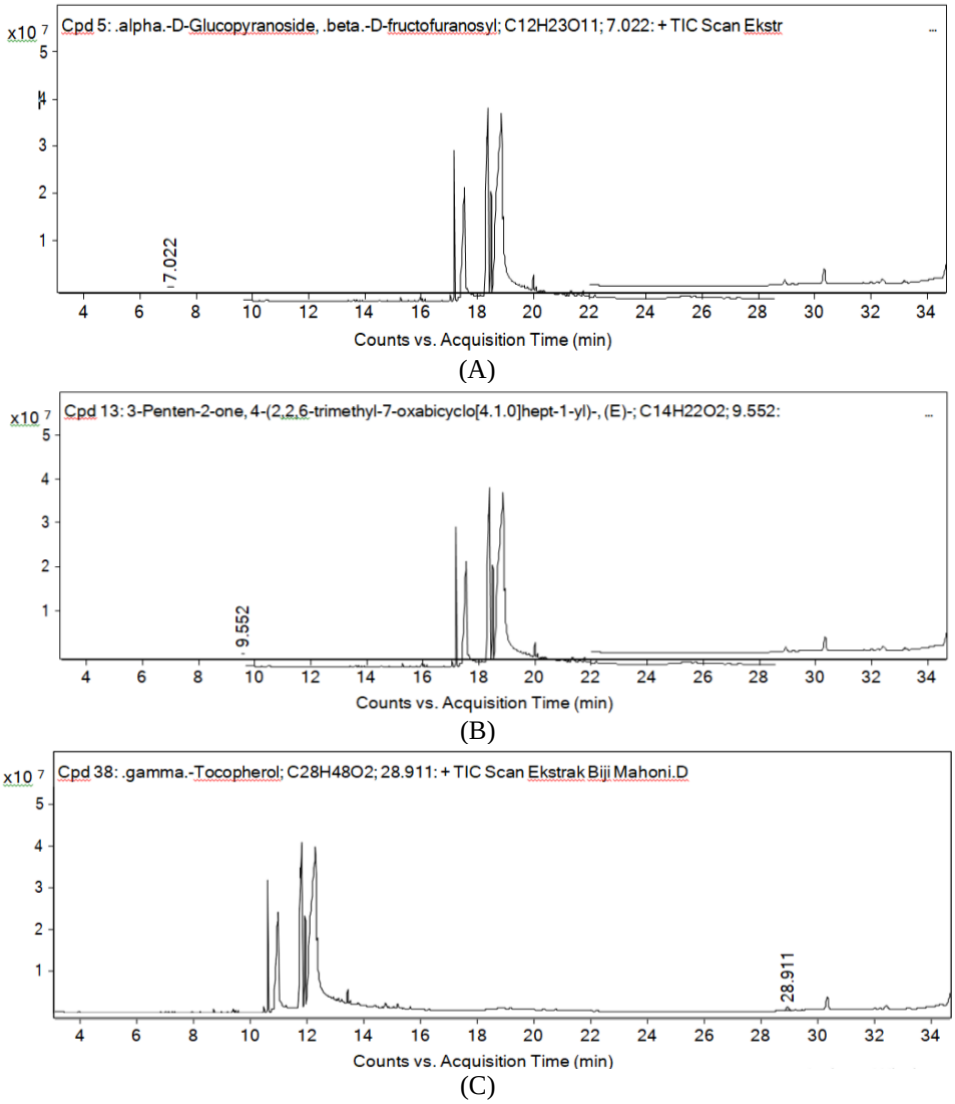

Fig. 2. RT Peak of secondary metabolite from Mahogany seeds A) *alpha-D Glucopyranoside*; B) *3-penten-2-one,* C) *gamma-Tocopherol*

Table 2. Screening result of secondary metabolite from mahogany samples

Part of Plant	Secondary Metabolite					
	Flavonoids	Alkaloids	Saponins	Terpenoids	Steroids	Tannins
Leaves	+	-	+	+	+	+
Seeds	-	-	+	+	+	-
Stem barks	+	-	-	+	+	-

3.3. GC-MS Analysis

GC-MS is a method that combines Gas Chromatography (GS) and Mass Spectrophotography (MS) to identify different compounds in a particular sample. Specifically, chromatography as a separation method is combined with mass spectrometry as an effective identification approach. In this study, stem barks, leaves, and seeds extract of mahogany were subjected to GC-MS analysis

(Fig. 2). The compounds that were successfully read in seeds extract were alpha *D-Glucopyranoside, 3-Penten-2 -one,* and *Gamma-Tocopherol*. Additionally, compounds that were identified in the leaf extract were *(1R,2R)-1-Methanol-2-acetonitrile-4- cyclohexene mesylate and 2H-1- Benzopyran-6-ol,3,4 dihydro2,5,7,8-tetramethyl -2- (4,8,12-trimethyltridecyl)*. Regarding stem barks, the compounds were 1,2-Benzenediol, Phenol, 2-propyl, and alpha-D Glucopyranoside, as shown in Table 3.

Table 3. GC-MS result of Mahogany Seeds Extract

No	Compound	Formula	Retention Time (Minutes)	Derivative
1	*alpha-D Glucopyranoside,*	C12H23O11	7.022	Flavonoids
2	*3-penten-2-one,*	C14H22O2	9.552	Saponins
3	*gamma-Tocopherol*	C28H48O2	29.911	Flavonoids
	Total		46.484	

Table 2 shows that there are three different identified compounds in mahogany seeds extract, namely alpha-D Glucopyranoside and gamma-Tocopherol with a retention time of 7.022 and 29.911, respectively. The 3-penten-2-one which is a class of saponin compounds has 9.552 retention time. These results show that the total retention time for each compound found in mahogany seeds was 46.484.

Alpha-D Glucopyranoside compound, also known as trehalose, is used as a carbon and energy source in plants, animals, fungi, and bacteria according to Akin [17]. Trehalose functions as an anti-oxidant which cleans free radicals [18], while 3-penten-2-one is a derivative of the saponin compound. Bera et al. [19] stated that mahogany seeds have functional capabilities due to the presence of bioactive components, including saponins. Moreover, the extraction of bioactive components of mahogany seeds could be carried out to facilitate their use as functional plants. Based on GC-MS analysis, the results showed several compounds that have high anti-viral and antioxidant potential, as presented in Table 4. These compounds are listed in Table 3, while GC-MS results are shown in Fig. 3.

Table 4. GC-MS Result of Mahogany Seeds Extract Potential as COVID-19 Medication

No	Compounds	Formula	Retention Time	Derivatives
1	*n-Hexadecanoic acid*	C16H32O2	10.975	Fatty Acid
2	*9,12-Octadecadienoic acid*	C18H32O2	11.787	Fatty Acid
3	*Squalene*	C30H50	21.633	Terpenoid
4	*Stigmasterol*	C29H48O	33.178	Steroid

The n-Hexadecanoic acid compound Based on Dr. Duke's phytochemical and ethnobotanical databases in Yarazari and Jayaraj [20], *n-Hexadecanoic acid* is a palmitic acid that can function as antioxidant and antiviral. According to Krishnamoorthy and Subramaniam [21], *9,12-Octadecadienoic acid* has benefits as antiviral, antibacterial, and anti-cancer. *Squalene* extracted from pumpkin seeds oil in the form of microemulsion has also been reported as an effective medication for COVID-19 which reduces fever for 2 days ($p = 0.025$), alleviates cough ($p = 0.010$),

and improves lung high-resolution computed tomography (p = 0.033) [22].

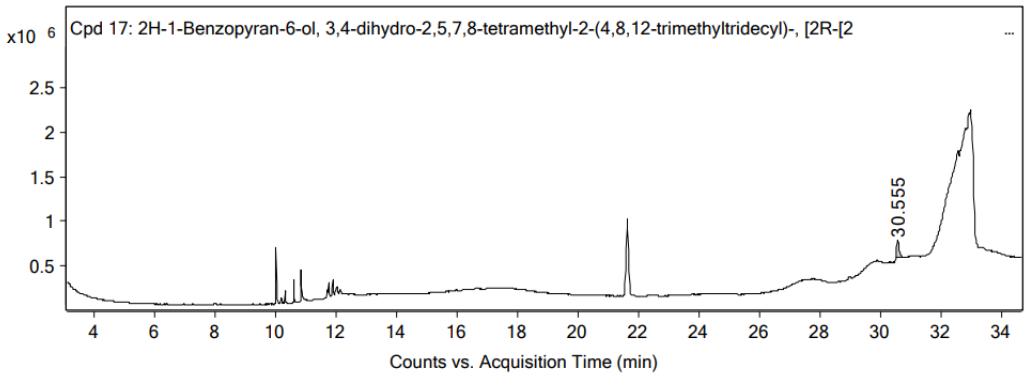

Fig. 3. RT peak compound of *2h-1-Benzopyr*

Table 5. GC-MS result of Mahogany leaves Extract

No	Compound	Formula	Retention Time	Derivatives
1	*2H-1-Benzopyran-6-ol,*	C29H50O2	30.555	Flavonoids
	Total		30.555	

Table 5 shows that only one compound from flavonoids is identified in mahogany leaves extract, namely 2H-1-Benzopyran-6-ol with a retention time of 30,555. Moreover, 2H-1-Benzopyran-6-ol is a phenolic compound classified as flavonoids. This compound is found in many plants providing numerous benefits for humans. According to Taiz and Zeiger [23], the flavonoid group (1,2H- benzopyran) shows antimicrobial activity, including anti-virus, urine laxative (diuretic), and anti-seizure. In the leaves of mahogany plant, there are several compounds that also have benefits as antioxidants for the body but are not included in the Flavonoid, Alkaloid, and Saponin groups. These compounds are alpha humulene, *neophytadiene, n-Hexadecanoic acid*, 9-Octadecenoic acid, and Octadecanoic acid which are a group of terpenoids and fatty acids (Table 6).

Table 6. GC-MS analysis from leave extract Mahogany potential for COVID-19 medication

No	Compound	Molecule Formula	Retention Time	Metabolite
1	*alpha humulene*	C15H24	7.243	Terpenoids
2	*neophytadiene*	C20H38	10.31	Diterpenoid
3	*n-Hexadecanoic acid*	C16H32O2	10.827	Fatty Acid
4	*9-Octadecenoic acid*	C19H36O2	11.732	Fatty Acid
5	*Octadecanoic acid*	C18H36O2	12.12	Fatty Acid
6	*Squalen*	C30H50	21.614	Terpenoids

The compound α-humulene, also known as α-karyophyllene, is an open-ring isomer of β-karyophyllene. Previous studies have shown the antibacterial potential of α-humulene, although its activity is related to other antibacterial compounds. Zhang et al. [24] stated that the main components of M. repandus essential oil were obtained from the sesquiterpene and oxygenated sesquiterpene groups. These groups have good antibacterial activity, increasing antimicrobial effects, broadening the antimicrobial spectrum, inhibiting drug resistance, and reducing adverse/toxic side effects.

Neophytadiene is a diterpene group compound, while diterpenes belong to terpenoids. Previous GC-MS analysis has shown that neophytadiene is a bioactive compound with anticancer activity, found in the ethyl acetate extract of Monoica Roxb leaves [25]. According to Sushmitha et al. [26] octadecanoid acid, tetradecanoid acid, 9,12,15-octadecatrienoic acid, 10,6,10, and nanonoic acid at a retention time of 9.454 function as anti-constipation, anti-inflammatory, antiviral, antimicrobial immunosuppressant, anticancer, hepatoprotective, anti-arthritic, anti-asthma, diuretic.anti-malarial, anti-dengue, anti-filariasis, and antimicrobial.

3.4. Result Analysis of GC-MC on Mahogany Stem Barks

GC-MS analysis from mahogany stem barks is shown in Fig. 4.

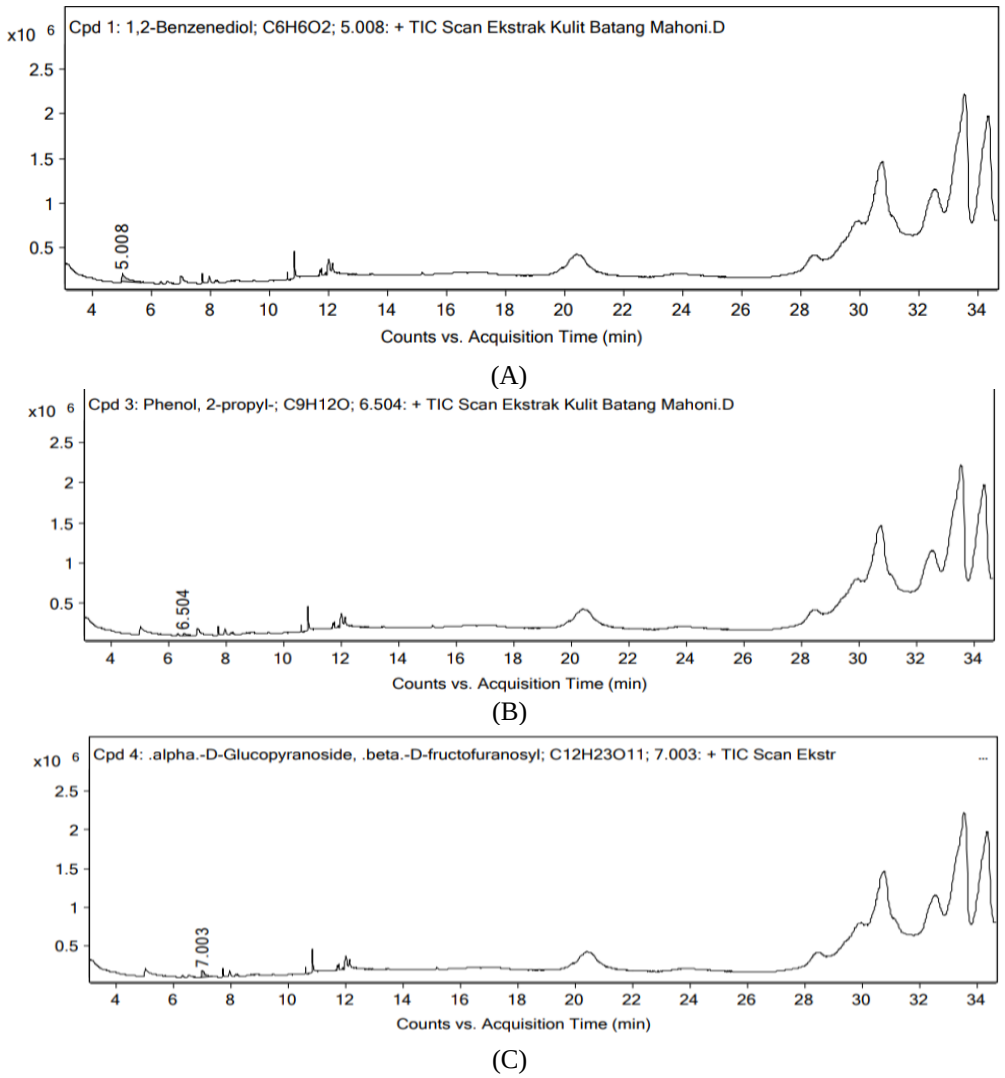

Fig. 4. RT Peak of secondary metabolites from Stem Barks; A) *1,2 Benzenediol; B) Phenol; C) alpha-D Glucopyranoside*

Table 7 shows the 3 compounds identified in mahogany stem barks extract sample, which belong to the group of flavonoids. These compounds include 1,2-Benzenediol, phenol, and alpha-D Glucopyranoside, with a retention time of 5,008, 6,504, and 7,003. The result obtained was that the total retention time for each compound found in mahogany stem barks was 18,515. Pyrocatechol, also known as 1,2-benzenediol or 2-hydroxyphenol, belongs to the organic

compounds known as catechols. Specifically, 1,2 benzenediol is flavonoid compound that can be used in the health and agricultural sectors. It is capable of inhibiting cell growth in breast cancer cell lines. The compound also has antibacterial properties that can be used in agriculture to control plant diseases caused by bacteria such as the phytopathogenic genera Xanthomonas, Ralstonia, and Acidovorax [27]. Treatment with catechol-induced DNA break, apoptosis G1 phase, and reduced protein expression related to G1-S progression [28].

Table 7. GC-MS Result from Stem Barks Extract of Mahogany

No	Compound	Formula	Retention Time	Derivatives
1	*1,2-Benzenediol*	C6H6O	5.008	Flavonoids
2	*Phenol*	C9H12O	6.504	Flavonoids
3	*alpha-D Glucopyranoside*	C12H23O11	7.003	Flavonoids
	Total		18.515	

Phenol is a compound from the flavonoid family that has the potential to be antiviral and antibacterial by denaturing cell proteins. Disturbed permeability of the cell wall and cytoplasmic membrane can cause an imbalance of macromolecules and ions in the cell, leading to lysis [29]. Alpha-glucosidase is an enzyme that catalyzes the cutting of glycosidic bonds in oligosaccharides. Additionally, it is a synthetic phenolic compound from flavonoids that acts as antioxidants in the body to avert free radicals. Studies have established that free radicals are the cause of various chronic diseases, including COVID-19. Alpha-glucosidase can also be applied as an antidiabetic agent, which is useful in preventing and protecting (prophylaxis) against diabetes mellitus [30].

4. Conclusion

In conclusion, this study showed that mahogany seeds extract had the highest retention time of 46,484 based on GC-MS analysis. Extract contained compounds in the form of alpha-D Glucopyranoside, 3-penten-2-one, and gamma-Tocopherol which were identified as flavonoids and saponins with COVID-19 medication. Other compounds contained terpenoids, steroids, and fatty acids with similar potential as COVID-19 medication, including alpha humulene, neophytadiene, n-Hexadecanoic acid, 9-Octadecenoic acid, Octadecanoic acid, Squalene, and Stigmasterol.

Abbreviations

GC-MS Gas Chromatography and Mass Spectroscopy
WHO World Health Organization
SAR-COV2 severe acute respiratory syndrome- coronavirus-2
MERS Middle East Respiratory Syndrome
CXI Chest x-ray Images
PCLD Post-*C*OVID-19 Lung Disease
TRC *Total Respond Chromatogram*

Data availability statement

Data will be shared upon request by the readers.

CRediT authorship contribution statement

Ifan Aulia Candra: Writing – Original draft, Conceptualization, Methodology, Resources, Formal analysis, Investigation, Data curation, Funding acquisition, Writing – review & editing, Project administration. Syahbudin Hasibuan: Validation, Data curation, Conceptualization. Fastabiqul Khoir: Conceptualization, Data curation, Formal analysis, Investigation.

Declaration of Competing Interest

The authors declare no competing financial interests or personal relationships could have appeared to influence the work reported in this study.

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