ISOLATION AND DETERMINATION OF CHEMICAL COMPOUNDS FROM N-HEXANE FRACTION OF THE SINTOK STEM BARK (*Cinnamomum sintoc* Bl.)

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ABSTRACT

It was reported that all fractions of *Cinnamomum sintoc* methanol extract had antioxidant properties which could delay, slowed down and prevented the occurrence of oxidation reactions caused by free radicals that could trigger degenerative diseases such as cancer, diabetes, and liver. This study aims to isolate and determine chemical compounds from n-hexane fraction of Sintok (*C. sintoc* Bl.) stem bark. The material was macerated using ethanol 70% followed by fractionation using n-hexane and water solvent. Phytochemical screening was performed to the hexane fraction. Vacuum liquid chromatography (VLC) was used to separate and isolate compounds using and preparative thin layer chromatography. The obtained isolates called FH_{3.2} and FH_{3.3} and determined using UV and IR spectrophotometers and Gas Chromatography-Mass Spectrometry. The ultraviolet spectrum of FH_{3.2} isolate showed the maximum wavelengths of 208, 229, and 275 nm. The infrared spectrum showed the presence of O-H, C-H aromatic groups, C = C, and C-O. The mass spectrum gave m / z: 164 [M+], 149, 131, 121, 103, 91, 77, 55, 51 having 97% similarity with eugenol. The ultraviolet spectrum of FH_{3.3} isolate showed a maximum wavelength of 206 nm. The infrared spectrum showed the presence of O-H, C = C, and C-O groups. The mass spectrum gave m/z: 222 [M+], 208, 189, 161, 147, 135, 121, 105, 93, 81, 67, 43 having 85% equality with juniper camphor. It could be concluded there were two dominant compounds of the fraction of n-hexane of the Sintoc stem bark i.e eugenol and juniper camphor.

Keywords: *Cinnamomum sintoc*, Sintok, Eugenol, Juniper Camphor, GC-MS.

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INTRODUCTION

Sintok plants (*Cinnamomum sintoc* Bl.) include the Lauraceae family, grown in West and Central Java, Malaysia and Thailand. The sintok (Indonesian) bark has a smooth texture, rather mild, soft, somewhat dense, grayish-brown red color, aromatic smell. The bark is empirically used by the public for the treatment of intestinal worms, murine drugs with seizures, wounds and swelling due to animal bites, dysentery, thrush, and fragrance¹⁻⁵. Based on research conducted by BPOM, a bark of sintok contains phenylpropanoid or alkenyl benzene compounds⁶. In addition, Phutdhawong stated that the main content of the essential oil of sintok leaf is linalool (36.90%) and cadinol (7.03%)⁷. In a study conducted by Sunardi *et.al* reported that the main content of the synthetic bark is eugenol and safrol⁸. Groups of compounds such as eugenol and safrol have been found to have an analgesic and anti-inflammatory effect⁹. In 2014, Alfira in her thesis stated that all fractions (water, ethyl acetate, and hexane fractions) have antioxidant activity by using DPPH (1,1-diphenyl, 2- picrylhydrazyl)¹⁰. It is reported that all fractions of *C. sintoc* methanol extract have antioxidant properties. It is understood that antioxidant compounds can delay, slow down and prevent the occurrence of oxidation reactions caused by free radicals that can trigger degenerative diseases such as cancer, heart, arthritis, diabetes, and liver. These antioxidant properties will be known if we know the compounds contained in the plants under study⁹.

The aim of this study was to report the compounds contained in the *C. sintoc* n-hexane fraction along with the isolation method and the appropriate determination to obtain the compound. Another faction analysis

will be presented in our other reports. The compounds obtained can then be verified whether they are antioxidants as anti-cancer by using the in-silico or in-vitro using cell-line methods¹¹⁻¹⁵.

EXPERIMENTAL

Material and Methods

Sample Collection

Dried sample of sintok was purchased from the Manoko Experimental Garden, Lembang, West Java, verified at the Laboratory of Taxonomy, Biology Department, Faculty of Mathematical and Physical Sciences, Universitas Padjadjaran

Extraction and Fractionation

Sintok powder was extracted using macerator equipment with 70% ethanol as a solvent based on Mustarichie *et.al* method^{16,17}. The resulting filtrate was concentrated by rotary vacuum evaporator (Rotavapor, Buchi RII) and then evaporated on a water bath at 50°C till constant weight to obtain the viscous ethanol extract. The extract was fractionated using liquid-liquid extraction with n-hexane and water solvent following modification of Mustarichie *et.al* method¹⁷.

Phytochemical Screening

Phytochemical screening of extracts and fractions using modifications of the Farnsworth method¹⁸. Actually, the phytochemical test was a procedure carried out by many researchers in evaluating plants that were thought to have medicinal effects^{19,20}.

Fractionation and Determination of Extracts

Vacuum Liquid Chromatography (VLC): VLC was used to separate and isolate desired fractions. The n-hexane fractional was introduced into the VLC column and eluted with methanol: chloroform mixture with multilevel polarization. Each subfraction was tested by TLC with a suitable developer to obtain a spot. The TLC used a stationary phase of silica gel GF254 and its mobile phase of chloroform: methanol with a variation. The VLC method was guided by Indonesian Herbal Pharmacopoeia²¹.

Purification and Purity Isolate Test

Purification was done by recrystallization using methanol. The crystals contained in the vials were dissolved with methanol and the exterior of the vial was soaked in warm water with a temperature range below 40°C while rocking slowly. Then, directly inserted into cold water, not to be submerged or water went into the vial. The isolate purity was tested by using two-way TLC. The stationary phase was used in the form of silica gel 60 with two different mobile phase systems.

Detection Method

The resulting isolates were then identified and determined by ultraviolet-visible spectrometry UV-Vis (Shimadzu UV 1800U), Spectroscopy FT-IR spectrometry (Shimadzu 8400), and GC-MS (Shimadzu QP 2010SE).

RESULTS AND DISCUSSION

Plant Determination

The result of plant determination indicated that simplicia was stem bark of sintok (*Cinnamomum sintoc* Bl.).

Results of Plant Materials Processing and Microscopic Analysis

Microscopic characteristics of the sintok stem bark powder were indicated by the presence of stone cells, oxalic crystals, oil cells, sclerenchyme fibers, and sclereids.

Extraction

The results of simplicia extraction of the bark of sintok produced a thick brown condensed extract of 9.03% of the weight of the dried sample.

Fractionation

The result of fractionation obtained by n-hexane fraction resulted in 10.48% and water fraction yield of 89.51%. The n-hexane fraction was thick yellowish brown oil with brown-green precipitate with an aromatic distinctive odor. Water fraction in the form of thick red-brown extract.

Phytochemical Screening

Phytochemical screening was performed on extracts and fractions. The results of phytochemical screening of the extract, n-hexane and water fractions of sintok bark can be seen in Table-1.

Table-1: Phytochemical Screening of Extract, n-Hexane and Water Fractions of *C. sintoc*

Compounds	Ethanol Extract	n-Hexane Fraction	Water Fraction
Alkaloids	-	-	-
Flavonoids	-	-	-
Tannin	+	+	-
Polyphenols	+	+	+
Monoterpenoid and sesquiterpenoid	+	+	+
Steroid	-	-	-
Triterpenoid	+	+	-
Quinone	+	-	+
Saponins	-	-	-

Notes : (+) : Detected, (-) : Not detected

Thin Layer Chromatography (TLC)

The thin layer extract chromatography was performed using silica gel 60 F254 silicone phase, toluene: ethyl acetate (93: 7) developer and detected using 366 nm, 254 nm UV lights and vanillin-sulfuric acid. The results of TLC of sintok bark extract can be seen in Table-2.

Table-2: TLC of Ethanol Extract of *C. Sintoc*

Spotting to-	Rf	UV Light		Vanillin-Sulphuric Acid
		254 nm	366 nm	
1	0.96	purple	purple	-
2	0.90	purple	-	purple
3	0.79	-	Yellow	-
4	0.65	-	-	purple
5	0.61	purple	purple	red-brown
6	0.51	purple	-	blue
7	0.40	purple	light blue	purple
8	0.31	-	-	blue
9	0.28	-	orange	purple
10	0.17	purple	orange	purple
11	0.09	-	-	purple
12	0.00	-	-	red

TLC of n-Hexane Fraction

Thin layer chromatography of the n-hexane fraction was carried out using silica gel 60 F254 silicone phase, the developer of n-hexane: ethyl acetate (9:1) and detected using 366 nm UV, 254 nm UV lights and vanillin-sulfuric acid. 15 spots were shown on the TLC plate (see Table-3).

Table-3: Vacuum Liquid Chromatography (VLC) Result of n-Hexane Fraction

Fraction	Organoleptic	Weight (mg)	Yields (%)
FH ₁	creamy yellow-orange oil, distinctive smell	318.5	6.00
FH ₂	yellowish oil, distinctive smell	407.9	7.69
FH ₃	thick orange oil, aromatic smell	1625.3	30.66
FH ₄	thick greenish oil, smelly	479.6	9.04
FH ₅	thick green brown oil	309.0	5.83
FH ₆	yellow brownish oil	315.4	5.95

Separation of the n-Hexane Fraction Component

Separation of the n-hexane fraction component was performed using VLC resulting in 30 fractions. The fraction monitored the pattern of spotting through TLC to see the similarity of spotting patterns of each fraction. A fraction with the same spotting pattern was combined so that six major fractions of n-hexane (FH₁ - FH₆) were obtained.

Purification of Compounds

Purification of FH₃ was done using preparative TLC. FH₃ was further isolated because it had relatively more yields and had a strong aromatic distinctive odor similar to pepper and cloves. The results of preparative TLC FH₃ can be seen in Table-4.

Table 4: TLC Preparative of FH₃

Bands	Rf	UV 366 nm	Vanillin-Sulphuric Acid
FH ₃₋₁	0.88	Light blue	-
FH ₃₋₂	0.60	dark purple	red-brown
FH ₃₋₃	0.42	-	purple
FH ₃₋₄	0.28	Light blue	-
	0.29	-	blue

Compounds Purity Test

TLC 2-dimensional isolate FH₃₋₂ produced single purple patches under 366 nm UV light and brown-red after sprayed with vanillin-sulphuric acid whereas isolate FH₃₋₃ produced purple single spots sprayed with vanillin-sulphuric acid spray. This indicated that the isolates FH₃₋₂ and FH₃₋₃ had been relatively pure.

Spectrophotometry Ultraviolet

Isolates FH₃₋₂ and FH₃₋₃ were identified using ultraviolet spectrophotometry at 200-300 nm wavelength intervals in methanol solvent. Isolate FH₃₋₂ showed the maximum wavelength (λ_{maks}) 208, 229, and 275 nm whereas FH₃₋₃ isolate showed λ_{max} 206 nm. The maximum wavelength at 208 nm was thought to arise from the electronic transition of the isolated double bond while the maximum wavelength at 229 and 275 nm was thought to arise from the electronic transition of the conjugated double bond^{22,23}. The ultraviolet spectrum of FH₃₋₃ isolate gave λ_{maks} at 206 nm. From this wavelength, it was suspected that there was an electronic transition from an isolated double bond²².

Infrared Spectrophotometry

Isolates FH₃₋₂ and FH₃₋₃ were identified using infrared spectrophotometry at 4500 - 500 cm⁻¹ wavenumbers on potassium bromide discs. The results of infrared spectrophotometry identification of FH₃₋₂ and FH₃₋₃ isolates can be seen in Table-5 and 6.

Table-5: IR Results of Isolate FH3-2

Wavenumbers (cm ⁻¹)	Shape band	Intensity	Presumption
3450	wide	medium	stretch O-H
3087	sharp	weak	stretch C-H aromatic
3028	sharp	weak	stretch C-H aromatic
2925	sharp	strong	stretch C-H aliphatic symmetry
2857	sharp	medium	stretch C-H aliphatic asymmetry
1740	sharp	medium	stretch C=C
1594	sharp	medium	stretch C=C aromatic
1454	sharp	medium	bend C-H aliphatic
1128	sharp	medium	stretch C-O alcohol tertiary

Isolates were analyzed using infrared spectrophotometry to determine functional groups contained in isolated molecules. The infrared spectra of FH₃₋₂ isolate showed an O-H strain of 3450 cm⁻¹. The absorption bands at 3087 and 3028 cm⁻¹ with weak intensity were thought to arise from the aromatic C-H strain

reinforced by the presence of an aromatic C = C strain of 1594 cm^{-1} . The absorption bands at 2925 cm^{-1} and 2857 cm^{-1} were thought to be derived from the symmetric and asymmetric C-H sp^3 stretches reinforced by the aliphatic C-H strain band of 1454 cm^{-1} . The absorption band at 1740 cm^{-1} was thought to be derived from the C = C strain. The medium-intensity absorption bands at 1128 cm^{-1} were thought to originate from the C-O strain on tertiary alcohol ^{24, 25}.

The infrared spectra of FH₃₋₃ isolate showed an O-H strain of 3434 cm^{-1} . The absorption bands at 2937 cm^{-1} and 2863 cm^{-1} were thought to originate from the symmetric and asymmetric C-H sp^3 strains reinforced by an aliphatic C-H strain of 1460 cm^{-1} . The absorption band at 1711 cm^{-1} was thought to be derived from the C = C strain. The absorption bands at 1113 cm^{-1} wave numbers were thought to originate from the C-O strain on tertiary alcohols. The absorption bands at 1062 cm^{-1} were thought to originate from the CH₂ strain in the terpenoid cyclic system ^{23, 30}.

GC-MS

Based on the gas chromatographic analysis, isolates FH₃₋₂ and FH₃₋₃ had retention time of 19,248 and 20,345 min respectively. From the mass spectrum, it was known that the FH₃₋₂ isolate had a molecular weight of 164 with the molecular structure of C₁₀H₁₂O₂. Isolate FH₃₋₂ had a m/z fragmentation pattern (relative intensity): 164 (100, base peak), 149 (37), 131 (32), 121 (19), 103 (39), 91 (36), 77 (51), 55 (46), 51 (30). The mass spectral pattern of FH₃₋₂ was similar to the eugenol mass spectrum pattern with a 97% equity index. Based on the mass spectra, it was known that the isolate FH₃₋₂ has a molecular weight of 164 (M+, 100) with M + 1: 165 (10.41) and M + 2: 166 (0.94) so that the isolates were thought to have the molecular structure C₁₀H₁₂O₂¹⁷. From the molecular structure, FH₃₋₂ isolate had a DBE value (double bond equivalent) of 5 so it was suspected to have a base frame consisting of one aromatic ring and one double bond. This basic framework was reinforced by fragments of m/z ions 77 derived from C₆H₅ ions and m/z 91 ion fragments derived from tropillary ions (C₇H₇) and in the presence of an m/z 55 ion fragment derived from C₄H₇ ion fragments in the mass spectrum. The mass spectra of isolates had similarities with the mass spectrum of eugenol with a 97% equity index. To confirm the identity of FH₃₋₂ isolates it is necessary to compare FH₃₋₂ isolates with eugenol based on the literature.

Organoleptically isolate FH₃₋₂ in the form of yellow liquor was almost colorless and smells the aromatic typical aroma of clove. This organoleptic had a resemblance to the organoleptic eugenol which was a colorless or slightly yellow liquid with the scent of cloves ²⁶. The ultraviolet spectrum of FH₃₋₂ isolate showed some similarities to the eugenol ultraviolet spectrum. Comparison of ultraviolet spectra of isolates FH₃₋₂ and eugenol based on literature can be seen in Table 7. From the data of ultraviolet spectrum comparison results, it could be seen that λ_{max} isolates FH₃₋₂ and eugenol had similar values except for λ_{max} 208 nm in isolates. The maximum wavelength at 208 nm was not included in the probability library because it was not a typical λ_{max} for the eugenol compound. The infrared spectra of FH₃₋₂ isolate had absorption bands which were also owned by eugenol. Comparison of infrared spectra of isolates FH₃₋₂ and eugenol based on literature can be seen in Table 8. Differences in the results of the infrared spectrum comparison appear from the relative shape and intensity of the bands. This difference might be due to differences in the measurement method and the infrared spectrophotometer used. Suspected identities of isolates FH₃₋₂ were reinforced by the similarity of mass spectra of isolates FH₃₋₂ with eugenol. Comparison of the fragmentation pattern of a mass spectrum of isolates FH₃₋₂ and eugenol based on literature can be seen in Table-9. Previous studies have also shown that eugenol was one component of the sintok bark ^{6, 8}. In addition, some literature also showed that eugenol was a common component of the genus Cinnamomum.^{25, 26} From the mass spectrum, it was known that the isolate had a molecular weight of 222 (M+, 100) with M+ 1: 223 (26.66) and M + 2: 224 (1.50) so that the isolates were thought to have the molecular structure of C₁₅H₂₆O ¹⁷. Of the molecular structure, FH₃₋₃ isolate had a DBE value of 3 so it was thought to have a base frame consisting of one double bond and two cyclic structures. The presence of double bonds was amplified by the absorption band at 1515 cm^{-1} in the infrared spectrum and the presence of λ_{max} at 206 nm indicating the presence of a double bond isolated. While the existence of two cyclic structures was supported by the absorption bands at 1062 cm^{-1} derived from the CH₂ strain on the terpenoid cyclic system $27\text{ }1070\text{ cm}^{-1}$ as well as the pattern of fragmentation of the isolated mass which was similar to the mass fragmentation of sesquiterpenoid compounds having two cyclic structures.³¹⁻³³ The presence of

cyclic structures was also supported by the fragment of m/z 55 (1,3-butadiene) suspected to arise as a result of a Diels-Alder retro reaction occurring on an unsaturated cyclic ring ²². In addition, the results of the phytochemical screening of the n-hexane fraction also showed the presence of sesquiterpenoid compounds. Comparison of FH₃₋₃ isolate mass fragmentation with some sesquiterpenoid compounds can be seen in Table-10. FH₃₋₃ isolate mass spectrum had a similarity index of 85% with juniper camphor. Therefore, to ensure the identity of the isolates it was necessary to compare the isolates of FH₃₋₃ with juniper camphor based on the literature.

Table-7: Comparison of Ultraviolet Isolate Spectra FH₃₋₂ and Eugenol

Isolate FH ₃₋₂ λ_{maks} , nm	Eugenol ¹⁸ λ_{maks} , nm	Eugenol, NIST Spectra Database ¹⁹ λ_{maks} , nm
208	-	-
229	232	230
275	282	278

Table-8: Comparison of Infrared Spectra Isolates FH₃₋₂ and Eugenol

Isolate FH ₃₋₂			Eugenol (Spectra Database for Organic Compound) ¹⁸			Presumption
Wave numbers (cm ⁻¹)	Bands shape	Intensity	Wave numbers (cm ⁻¹)	Bands shape	Intensity	
3450	wide	medium	3618	Wide	medium	O-H
3087	sharp	weak	3077	Sharp	weak	C-H aromatic
3028	sharp	weak	3061	Sharp	weak	C-H aromatic
2925	sharp	strong	2939	Sharp	weak	C-H aliphatic asymmetry
2857	sharp	medium	2843	Sharp	weak	C-H aliphatic asymmetry
1740	sharp	medium	1738	Sharp	medium	C=C aromatic
1594	sharp	medium	1514	Sharp	strong	C=C olefinic
1454	sharp	medium	1452	Sharp	strong	C-H aliphatic
1128	sharp	medium	1122	Sharp	strong	C-O alcohol tertiary

Table-9: Comparison of Fragmentation Pattern of Isolates FH₃₋₂ and Eugenol

Isolate FH ₃₋₂		Eugenol (WILEY Spectra Database)	
m/z	relative intensity	m/z	relative intensity
164	100	164	100
149	37	149	37
131	32	131	32
121	19	121	18
103	39	103	39
91	36	91	36
77	51	77	50

Table-10: Comparison of Mass Fragmentation Patterns Isolate FH3-3 with Some Sesquiterpenoid Compounds²⁶⁻²⁸.

Compounds	Ion fragments (m/z)												
δ -selinen		204	189	175	161	147	133	119	105	91	81	67	55
Gorgonen		204	189	175	161	147	133	119	105	91	81	69	55
Sibiren		204	189	175	161	147	133	119	105	91	79	67	55
5-epi-aristolocen		204	189	175	161	147	133	119	105	91	79	67	55
Isolate FH ₃₋₃	222	204	189	175	161	147	133	121	105	93	81	67	55

Organoleptically isolate FH₃₋₃ in the form of a distinctive weak orange-yellow liquid. Juniper camphor itself was a compound belonging to the eudesmane sesquiterpene compound which was one of the essential oil components in some plant species such as *Garcinia* sp., *Callicarpa* sp. *Protium* sp. as well as on some

Araliaceae³⁴⁻³⁸. The alleged identity of isolates was reinforced by the similarity of the fragmentation pattern of FH3-3 isolate mass with juniper camphor. From the mass spectrum, it was known that FH3-3 isolate had a molecular weight of 222 (see Fig.-1) with C₁₅H₂₆O molecular structure. Isolate FH3-3 had a m/z fragmentation pattern (relative intensity): 222 (1), 208 (17), 189 (20), 161 (16), 147 (13), 135 (21), 121 (15), 105 (26), 93 (35), 81 (51), 67 (43), 43 (100, base peak). The mass spectral pattern of FH3-3 was similar to that of the juniper camphor mass spectrum pattern with an 85% equality index. Moreover, the alleged identity of isolates was also supported by previous studies which showed that juniper camphor was one component of the sintok bark.^{6, 8}

Fig.-1: Mass Spectrum of Isolate FH₃₋₃

Determination of chemical compounds from plants that use methods similar to the methods listed here has been carried out by many people. Raji *et.al*, for example, reported secondary metabolites like alkaloids, flavonoids, tannins, and saponins were extracted from four medicinal plants viz. *Cassia alata*, *Thespesia populnea*, *Euphorbia hirta*, and *Wrightia tinctoria* and characterized by UV, TLC, FTIR and GCMS analysis³⁹. Insanu *et.al* mentioned isolation non-alkaloid compounds in the *Cinchona. officinalis* bark using spectroscopic methods (UV, IR, ESI-MS, NMR (1H-, 13C-, HSQC, and HMBC)⁴⁰. Study in vitro antioxidant activity of isolated compound from methanolic stem extracts of *Jasminum auriculatum* was studied by Srivastava *et.al*⁴¹.

CONCLUSION

Based on phytochemical screening results, it was found that the n-hexane fraction of sintok bark (*Cinnamomum sintoc* Bl.) contained tannin, polyphenol, monoterpenoid and sesquiterpenoid and triterpenoids. From this fraction, isolates FH₃₋₂ and FH₃₋₃ were obtained. FH₃₋₂ isolate was obtained in the form of pale yellow liquid and typical aromatic odor similar to clove aroma while FH₃₋₃ isolate was obtained in the form of a weak yellow odor orange. Based on the analysis of the ultraviolet spectrum, infrared spectrum, GC-MS spectra, as well as the results of the comparison of literature data, FH₃₋₂ isolates were thought to be eugenol compounds while FH₃₋₃ isolates were thought to be juniper camphor compounds.

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