

Article

Effect of Growing Location on The Chemical Profile of The Essential Oil of Papua Nutmeg (*Myristica argentea* Warb.) based on GC-MS analysis

Article Info

Article history :

Received July 29, 2026

Revised October 10, 2026

Accepted October 16, 2026

Published October 30, 2026

In Press

Keywords :

Papua Nutmeg,
Myristica argentea,
essential oil,
phytochemistry,
growing location

Syefira Salsabila^{1*}, Imanuel Berly Delvis Kapelle², Dwi Anggara Putri Usman¹, Daniella Elizabeth Engel¹, Nini Munirah Renur³

¹Pharmacy Study Program, Department of Chemistry, Faculty of Science and Technology, Pattimura University, Ambon, Indonesia

²Chemistry Study Program, Department of Chemistry, Faculty of Science and Technology, Pattimura University, Ambon, Indonesia

³Fishery Product Technology Department, Tual State Fisheries of Polytechnic, Southeast Maluku, Indonesia

Abstract. *Myristica argentea* Warb. is an endemic Indonesian nutmeg species with potential as an economically valuable essential oil source. This study evaluated the effect of growing location on the chemical profile of *M. argentea* seed essential oil from two locations in Maluku: West Seram on Seram Island, characterized by inland mountainous forest, and Hutumuri on Ambon Island, a low-lying coastal area. Essential oils were obtained by steam distillation and analyzed using Gas Chromatography-Mass Spectrometry. The oil yields from West Seram and Hutumuri were 1.95% and 1.78%, respectively. Twenty compounds were identified in both samples, with sabinene as the dominant component (26.34% in West Seram and 32.75% in Hutumuri), followed by β -phellandrene, safrole, and (+)- α -pinene. Although qualitative composition was similar, quantitative differences were observed in several compounds, particularly sabinene, safrole, and myristicin. The contrasting environmental characteristics may be associated with variations in secondary metabolite biosynthesis and essential oil composition. The relatively high safrole content, particularly in Hutumuri, highlights the need for safety assessment and quality standardization before potential industrial applications. These findings provide baseline information on geographical variation in the chemical profile of *M. argentea* essential oil.

This is an open access article under the [CC-BY](#) license.



This is an open access article distributed under the Creative Commons 4.0 Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. ©2026 by author.

Corresponding Author :

Syefira Salsabila

Pharmacy Study Program, Department of Chemistry, Faculty of Science and Technology,

Pattimura University, Ambon, Indonesia

Email : syefira.salsabila@lecturer.unpatti.ac.id**1. Introduction**

Indonesia is a megadiverse country with exceptionally high plant diversity and a rich diversity of medicinal plants; however, ethnobotanical documentation remains geographically uneven, and many of these plants have yet to be scientifically explored [1]. This biological richness has encouraged the use of various plant species as traditional medicines that have been passed down through generations in Indonesia communities [2]. One plant of particular importance as both a spice and a medicinal plant is nutmeg. Nutmeg is a signature commodity of eastern Indonesia, particularly the Maluku Islands, and has long been recognized and utilized for its diverse uses and economic value. Its economic potential has driven the expansion of nutmeg cultivation through plantations across various regions of Maluku. Nutmeg essential oil is used as a raw material in the pharmaceutical, cosmetic, and beverage industries, while its leaves are used in various herbal spa products for relaxation [3-4].

Nutmeg (*Myristica fragrans* Houtt.) belongs to the family *Myristicaceae* and is an evergreen tropical tree with a characteristic aroma and flavor [5-6]. Nutmeg seeds contain 5-15% essential oil, which is widely used in the perfume and pharmaceutical industries [7]. Various studies have reported that nutmeg exhibits diverse biological and pharmacological activities, including antidysenteric, antibacterial, antifungal, antimalarial, larvicidal, antioxidant, anti-inflammatory, antiviral, antithrombotic, hepatoprotective, neurostimulatory, anticonvulsant, anticancer, aphrodisiac, stomachic, and nootropic activities [8-13].

In addition to common nutmeg (*M. fragrans*), Indonesia is also home to another endemic nutmeg species, Papua nutmeg (*M. argentea* Warb.), which grows naturally in the Papua region and the Maluku Islands [14]. This species is not yet as widely utilized commercially or studied scientifically as common nutmeg, despite its considerable potential as a source of bioactive compounds [15]. *M. argentea* shares similar morphological characteristics and growing conditions with *M. fragrans*, bears oval-shaped fruits, and all parts of the plant—including the flesh, seed, mace, and leaves—can be used in traditional medicine [16-17]. It possesses pharmacological activity as an antioxidant and antibacterial agent [18].

Essential oils are mixture of volatile aromatic compounds produced by plants that plays important role in plant defense mechanisms. In addition, essential oils are known to possess various biological activities with potential applications in health and industry [19]. The composition of secondary metabolites in plants is influenced by both internal and external factors. Internal factors are mainly related to genetics, while external factors include cultivation conditions, soil type, soil pH, nutrient content, temperature, light intensity, humidity, rainfall, altitude, geographical position, and harvest time [20-23]. Various studies have shown that essential-oil-producing plants can exhibit considerable variation in both the quality and quantity of the oil produced in response to the environmental conditions of their growing sites [24]. Different environmental conditions can also affect the accumulation and composition of secondary metabolites through changes in plant physiological and biosynthetic processes. Furthermore, variations in climatic conditions and abiotic factors can lead to differences in secondary metabolite accumulation among populations or growing locations [22].

Studying variation in secondary metabolites requires a metabolomic approach to obtain a comprehensive picture of the chemical composition of a sample. One widely used metabolomic approach is metabolic fingerprinting, which employs chromatographic and spectroscopic techniques to identify metabolite patterns in a sample [21]. This approach has been widely applied in the quality control of herbal materials, including geographical origin tracing, adulteration detection, and species authentication based on their chemical characteristics [25].

Various analytical techniques have been developed to identify and differentiate chemical composition of samples, one of which is Gas Chromatography–Mass Spectrometry (GC-MS) [26]. This technique is widely used in pharmaceutical research, forensics science, environmental science, and natural-product research because it can separate and identify individual chemical components based on their mass spectral characteristics [27-29]. GC-MS offers high sensitivity and resolution, enabling the detection of both volatile and semivolatile compounds, including metabolites present at low concentrations in complex matrices [26],[30].

Although several studies have reported the chemical composition of the essential oils from *M. fragrans*, information on the chemical profile of *M. argentea* essential oil remains relatively limited. Previous studies have characterized *M. argentea* essential oil from a single location [14] and used GC-MS fingerprinting combined with chemometric analysis to differentiate *M. argentea* and *M. fragrans* [16]. However, information on variations in the chemical profile of *M. argentea* essential oil among different growing locations within the same species remains limited, particularly in the Maluku region. Differences in habitats, such as inland forest and coastal environments, may result in distinct ecological conditions and potentially contribute to variations in secondary metabolite biosynthesis. Such environmental conditions have been reported to influence the biosynthesis of monoterpenes and phenylpropanoids in several aromatic plant species [31-32].

Based on this knowledge gap, this study was conducted to analyze and compare the chemical profile of the essential oil of Papua nutmeg seeds (*M. argentea* Warb.) collected from two different growing locations in Maluku using GC-MS analysis. The novelty of this study lies in its comparative assessment of the influence of growing location on the chemical composition of *M. argentea* essential oil, an Indonesian nutmeg species that remains underexplored, thereby addressing a specific gap that has not previously been investigated for this species. The findings of this study are expected to provide scientific information on the chemical profile variation of Papua nutmeg essential oil, support raw material quality standardization, and serve as a basis for developing the utilization of *M. argentea* essential oil in the pharmaceutical, food, cosmetic, and other biodiversity-based industries.

2. Experimental Section

2.1. Materials

The main material used in this study was Papua nutmeg seeds (*M. argentea* Warb.) obtained from two different locations in Maluku Province, namely West Seram, Seram Island (MA01), and Hutumuri, Ambon Island (MA02). The chemicals used included distilled water, n-hexane (pro-analysis grade), and anhydrous sodium sulfate (Na_2SO_4).

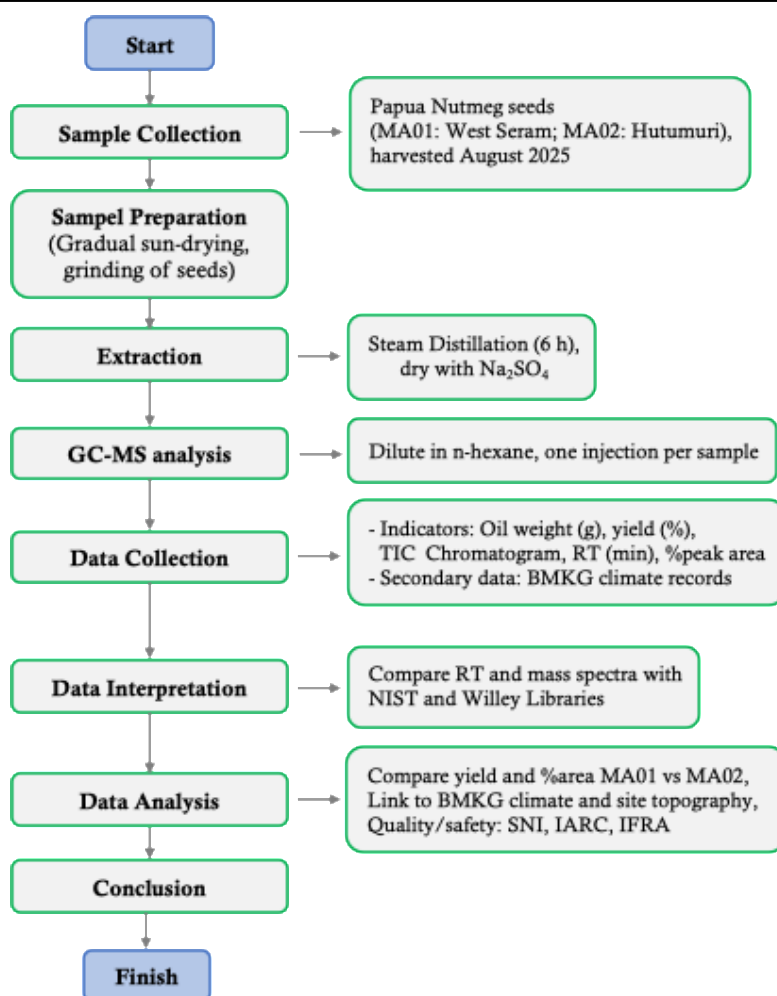


Figure 1. Schematic/Flowchart of research

2.2. Methods

2.2.1 Extraction of Papua Nutmeg Essential Oil (*M. argentea* Warb.)

Papua Nutmeg (*M. argentea*) seeds were harvested on August 2025, during the middle of the rainy season, and were subsequently dried by gradual sun-drying without direct exposure to intense sunlight. Whole, dry Papua nutmeg seeds were weighed at 1.3 kg for sample MA01 and 1.058 kg for sample MA02. The samples were then ground to reduce the particle size and increase the surface area for extraction. Essential oil extraction was carried out using the steam distillation method. Each sample was distilled once for 6 h. The resulting essential oil was separated from the aqueous phase and dried over anhydrous sodium sulfate to remove residual water. The essential oil was subsequently stored in a tightly sealed amber glass bottle, protected from light, until further analysis was carried out. The essential oil yield was calculated as the ratio of the weight of essential oil obtained to the dry weight of the sample and expressed as a percentage (%).

2.2.2 Chemical Profile Analysis Using Gas Chromatography-Mass Spectrometry (GC-MS)

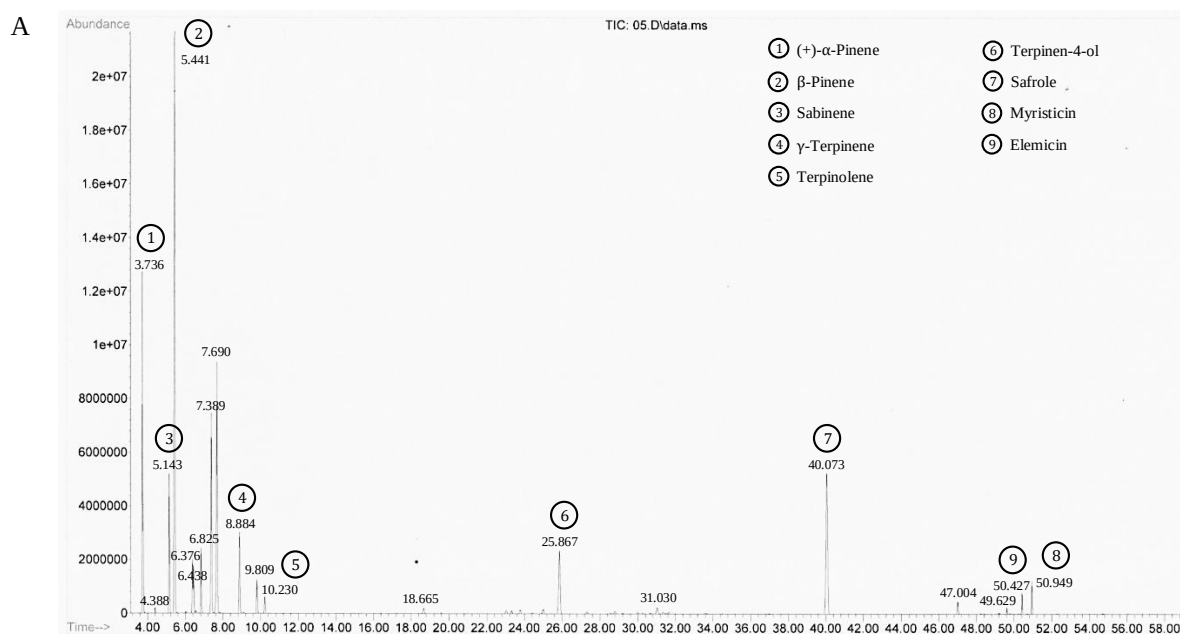
Chemical profile analysis of the essential oil was carried out using a GC-MS instrument to identify the volatile compounds contained in the essential oil of Papua nutmeg seeds (*M. argentea* Warb.). Each essential oil sample was analyzed once. Prior to analysis, the essential oil was diluted in n-hexane to an appropriate concentration and then injected into the GC-MS system. Compound separation was

performed using an HP-5MS capillary column (30 m $\times$ 0.25 mm $\times$ 0.25 μ m). Helium was used as the carrier gas at a constant flow rate of 1.0 mL min⁻¹. The injector temperature was maintained at 250°C and the detector temperature at 280°C. The oven temperature program started at 60°C and was held for 2 min, then increased at a rate of 5°C min⁻¹ up to 280°C, and held for 10 min. All detected compounds were quantified based on the percentage relative peak area (%). Compound identification was performed tentatively by comparing the relative retention times and mass spectra with the National Institute of Standards and Technology (NIST) and Wiley reference libraries integrated into the GC-MS system [33]. The identification results are presented as the compound name, retention time, and relative peak area percentage for each detected component.

3. Results and Discussion

The plant material used in this study consisted of dry Papua nutmeg seeds obtained from West Seram (SBB), Seram Island (MA01), and Hutumuri, Ambon Island (MA02). Extraction using the steam distillation method showed that the essential oil obtained from MA01 was 25.36 g with a yield of 1.95%, while MA02 yielded 18.83 g with a yield of 1.78%. These yield were higher than those reported by Maryati (2023) [14], who reported an essential oil yield of $1.35 \pm 0.13\%$ (v/w) for *M. argentea* seeds using water-steam distillation. The observed difference in yield may be attributed to differences in growing location and environmental conditions. Genetic and environmental factors such as temperature, rainfall, altitude, and soil fertility are known to affect the biosynthesis and accumulation of volatile compounds in plants [34-36].

GC-MS analysis of the Papua nutmeg essential oil resulted in total ion chromatograms (TICs), as presented in Table 1 and Figure 2. The chromatograms of both samples showed similar qualitative profiles, but differences in peak intensity were observed, indicating quantitative variation between locations. This indicates that although the compound composition is relatively similar, the proportion of each component appeared to vary between the two sampling locations.



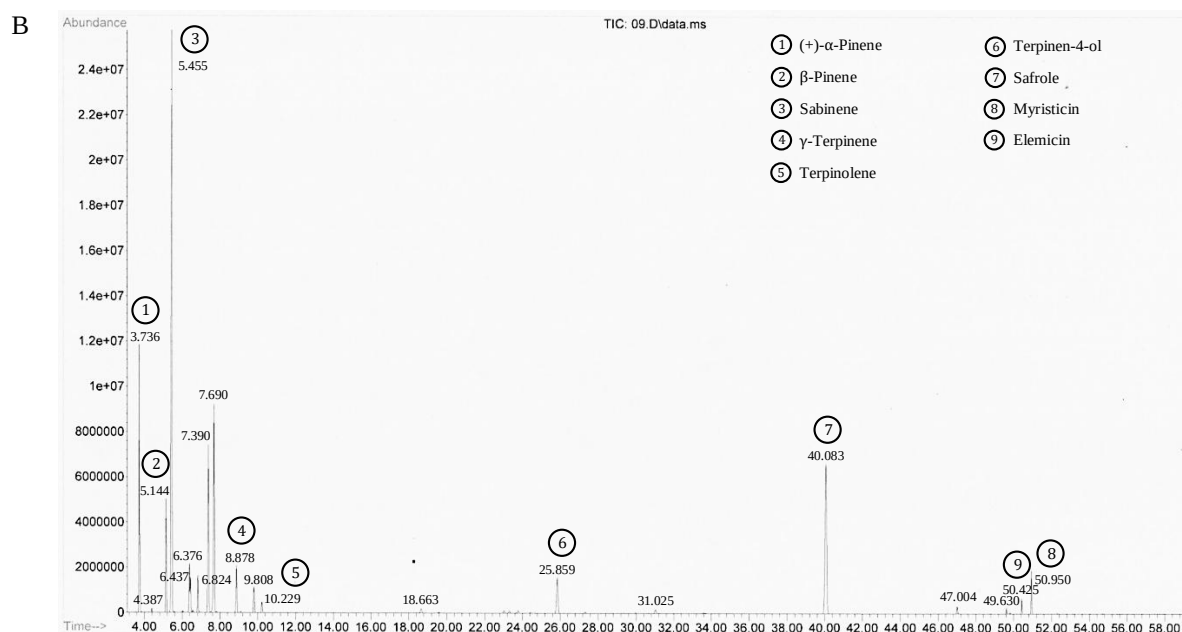


Figure 2. GC-MS chromatogram of essential oil extracted from Papua nutmeg seeds (*M. argentea* Warb.): A. MA01, Papua nutmeg from West Seram (SBB) – Seram Island; B. MA02, Papua nutmeg from Hutumuri – Ambon Island

Table 1. Characterization of the essential oil composition of Papua nutmeg seeds (*M. argentea* Warb.) using Gas Chromatography-Mass Spectrometry (GC-MS)

No.	Name of Compound (Molecular formula; CAS Number)	RT* (min)	Peak area percentage (%)	
			MA01	MA02
1	(+)-α-Pinene (C ₁₀ H ₁₆ ; 7785-70-8)	3.73	11.70	10.01
2	Camphene (C ₁₀ H ₁₆ ; 79-92-5)	4.38	0.18	0.16
3	β-Pinene (C ₁₀ H ₁₆ ; 127-91-3)	5.14	5.24	4.89
4	Sabinene (C ₁₀ H ₁₆ ; 3387-41-5)	5.45	26.34	32.75
5	β-Myrcene (C ₁₀ H ₁₆ ; 123-35-3)	6.37	2.16	2.16
6	α-Phellandrene (C ₁₀ H ₁₆ ; 99-83-2)	6.43	1.73	1.41
7	α-Terpinene (C ₁₀ H ₁₆ ; 99-86-5)	6.82	2.69	1.71
8	D-Limonene (C ₁₀ H ₁₆ ; 5989-27-5)	7.38	9.67	8.94
9	β-Phellandrene (C ₁₀ H ₁₆ ; 555-10-2)	7.69	12.90	11.79
10	γ-Terpinene (C ₁₀ H ₁₆ ; 99-85-4)	8.88	3.96	2.53

No.	Name of Compound (Molecular formula; CAS Number)	RT* (min)	Peak area percentage (%)	
			MA01	MA02
11	o-Cymene (C ₁₀ H ₁₄ ; 527-84-4)	9.80	1.78	1.49
12	Terpinolene (C ₁₀ H ₁₆ ; 586-62-9)	10.23	0.91	0.62
13	Sabinenehydrate (C ₁₀ H ₁₈ O; 546-79-2)	18.66	0.35	0.34
14	Terpinen-4-ol (C ₁₀ H ₁₈ O; 562-74-3)	25.86	4.90	3.01
15	α -Terpineol (C ₁₀ H ₁₈ O; 98-55-5)	31.02	0.47	0.32
16	Safrole (C ₁₀ H ₁₀ O ₂ ; 94-59-7)	40.08	12.33	14.38
17	Methyleugenol (C ₁₁ H ₁₄ O ₂ ; 93-15-2)	47.01	0.63	0.40
18	Eugenol (C ₁₀ H ₁₂ O ₂ ; 97-53-0)	49.62	0.20	0.22
19	Elemicin (C ₁₂ H ₁₆ O ₃ ; 487-11-6)	50.427	0.69	0.54
20	Myristicin (C ₁₁ H ₁₂ O ₃ ; 607-91-0)	50.95	1.16	1.74

*Retention time

Overall, 20 compounds were successfully identified in both samples. The dominant compounds included sabinene, β -phellandrene, safrole, and (+)- α -pinene, followed by β -pinene, γ -terpinene, terpinolene, terpinen-4-ol, myristicin, and elemicin. These compounds are the major constituents responsible for the characteristic aroma of nutmeg and are known to contribute to various biological activities, including antioxidant, antimicrobial, and anti-inflammatory activities [10][37-40].

Sabinene was the most abundant constituent in both samples, accounting for 26.34% in MA01 and 32.75% in MA02. Sabinene is a monocyclic monoterpene known to possess antimicrobial, antioxidant, and anti-inflammatory activities [41]. The higher sabinene content in MA02 indicates a possible influence of environmental conditions on the enhanced biosynthesis of certain monoterpene compounds, although this tendency requires confirmation through replicate analyses.

Safrole was detected as the second most abundant component, at 12.33% (MA01) and 14.38% (MA02). Safrole is a phenylpropanoid compound with various biological activities; however, it is also recognized for its genotoxic potential. The International Agency for Research on Cancer (IARC) classifies safrole as Group 2B (possibly carcinogenic to humans) based on evidence of carcinogenicity in experimental animals, particularly in relation to liver cancer [42-43]. Therefore, the relatively high safrole content in both samples, especially MA02, warrants careful consideration in the safety evaluation and standardization of *M. argentea* essential oil products.

Given that the European Commission has prohibited the addition of safrole as a pure flavoring substance in food products and has established maximum limits for its natural content in certain food products, such as soups, sauces, and non-alcoholic beverages [42], and that the International Fragrance Association (IFRA) restricts the total safrole content in cosmetic/fragrance products to a maximum of 0.01% in the final product [44], the safrole content in the essential oil of *M. argentea* MA02 (14.38%) clearly far exceeds these safety limits if used without further processing. Therefore, the utilization of *M. argentea* essential oil in the food, cosmetic, and pharmaceutical sectors requires

mitigation strategies, such as substantial dilution to below the applicable regulatory thresholds. The separation of the safrole-rich fraction through fractionation techniques may also serve as an alternative mitigation strategy for this class of alkenylbenzene compounds; however, specific validation on *M. argentea* essential oil is still required before this approach can be definitively recommended.

β -phellandrene was detected at 12.90% (MA01) and 11.79% (MA02), while (+)- α -pinene was detected at 11.70% (MA01) and 10.01% (MA02). (+)- α -pinene is a bicyclic monoterpene commonly found in essential oils and has been reported to exhibit anti-inflammatory activity [45]. β -phellandrene has also been identified as one of the major constituents of the essential oils of other aromatic plants, which have demonstrated antimicrobial activity against several anaerobic bacteria and *Candida albicans* [46]. The difference in the levels of these two compounds indicates variation in terpenoid biosynthetic pathways between growing locations.

Myristicin, one of the characteristic marker compounds of nutmeg essential oil, accounted for 1.16% in MA01 and 1.74% in MA02. This compound has been reported to exhibit promising pharmacological activities, particularly antioxidant, anti-inflammatory, and antiproliferative effects [47]. According to the Indonesian National Standard (SNI 06-2388-2006), myristicin content is generally used as a quality parameter for nutmeg oil, with a minimum value of 5% [48]. The myristicin content in both samples was below this standard and was also lower than the range of 2.12-5.98% reported by A'Mun [49].

However, this low myristicin content is consistent with patterns reported for other endemic Indonesian nutmeg species, using the same SNI analytical method, Karmanah et al (2020) [5] reported a myristicin content of only 1.3% in the seeds of Ambon Forest nutmeg (*M. fatua*), markedly lower than that of Banda nutmeg (*M. fragrans*, 8.72%), suggesting that the low myristicin content in *M. argentea* likely reflects a species-specific chemotype rather than an indication of inferior quality. This is further supported by chemotaxonomic evidence from Khamnuan et al. (2026) [16], who reported that *M. fragrans* is consistently characterized by high sabinene and pinene levels, whereas *M. argentea* is characterized by higher safrole levels, with myristicin serving as one of the key differentiating markers between the two species.

In addition to these major compounds, other monoterpenes were identified, including β -myrcene (2.16% in MA01 and 2.16% in MA02), α -phellandrene (1.73% and 1.41%), α -terpinene (2.69% and 1.71%), D-limonene (9.67% and 8.94%), and o-cymene (1.78% and 1.49%). Several minor constituents were detected in trace amounts, including camphene (0.18% and 0.16%), sabinene hydrate (0.35% and 0.34%), α -terpineol (0.47% and 0.32%), methyleugenol (0.63% and 0.40%), and eugenol (0.20% and 0.22%).

The differences in chemical composition between MA01 and MA02 may be attributed to environmental factors. Based on BMKG climatological data for the period February 2025-Januari 2026, the average air temperature and relative humidity of West Seram (Seram Island) and Hutumuri (Ambon Island) were relatively similar (27.1°C and 87.0% in West Seram; 26.8°C and 85.9% in Hutumuri), whereas total rainfall during this period was considerably higher in Hutumuri (6,126.2 mm) than in West Seram (3,298.6 mm) [50]. Topographically, Hutumuri is a gently sloping coastal area (elevation 0-50 m a.s.l) with coarse-textured soil (gravel and coral fragments) near the shoreline, transitioning to medium sand further inland [51], whereas West Seram is dominated by hilly-to-mountainous terrain with an average elevation of ~114 m a.s.l. and a clay-slit-sandy soil texture [52]. These difference in rainfall, elevation, and soil texture between the two locations are presumed to contribute to the observed variation in secondary metabolite biosynthesis.

Interestingly, the pattern of variation among individual compounds in this study was not uniform in relation to the differences in rainfall between the two locations. Most monoterpenes (10 of the 11 identified compounds) showed higher levels in West Seram (lower rainfall), consistent with findings by Lotfi et al. (2024) [53] in *Stachys lavandulifolia*, which demonstrated that variations in essential oil content and composition among populations were associated with environmental and edaphic

conditions. However, sabinene — the dominant component in both samples — along with Safrole and Myristicin, showed higher levels in Hutumuri (higher rainfall). This pattern is consistent with the findings of Martin et al. (2019) [54] in *Iryanthera polyneura*, where some terpenoids were more abundant during the rainy season, whereas others increased during the dry season. In contrast, Zamani et al. (2025) (55) reported that temperature and rainfall were not significantly correlated with essential oil composition in *S. lavandulifolia*, indicating that the influence of climatic factors is not always consistent. A similar variation in compound-specific responses has also been reported in another member of the *Myristicaceae* family, *Osteophloeum platyspermum*, in which certain groups of terpene compounds exhibited different patterns between the dry and rainy seasons [56]. These findings suggest that the effects of rainfall, elevation, and soil texture on secondary metabolite biosynthesis in *M. argentea* are compound-specific rather than representing a single uniform effect across all terpenoid and phenylpropanoid groups.

Environmental factors such as temperature water availability, light intensity, and soil conditions can influence the accumulation and composition of secondary metabolites by altering physiological processes and biosynthetic pathways in plants [23],[32],[35-36]. In the present study, the interpretation of the role of environmental factors provides an initial contextual framework based on regional climatological data and the geographical characteristics of the two locations rather than on direct measurements of environmental parameters. Therefore, further research incorporating direct measurements of meteorological parameters and soil physicochemical characteristics at the sampling sites is needed to provide a more comprehensive assessment of the relationship between environmental conditions and variations in the chemical profile of *M. argentea* essential oil.

4. Conclusion

This study identified 20 compounds in the essential oil of Papua nutmeg seeds (*M. argentea* Warb.) collected from two different growing locations using GC-MS. The major constituents included (+)- α -pinene, β -pinene, sabinene, β -phellandrene, γ -terpinene, terpinolene, terpinen-4-ol, safrole, myristicin, and elemicin. Quantitative differences in the relative abundances of several constituents were observed between the two locations, particularly for sabinene, safrole, and myristicin, which were higher in the sample from Hutumuri (Ambon Island). These differences may be attributed to environmental factors such as rainfall, elevation, and soil texture between the two locations. However, since each sample was analyzed by a single GC-MS injection, these differences should be regarded as preliminary indications rather than statistically validated distinctions. The higher safrole content found at one location (Hutumuri, Ambon Island) underscores the need for standardization and quality control to ensure the safe use of Papua nutmeg essential oil. Further studies are needed to include additional growing locations, include analytical replication and to investigate the pharmacological and toxicological properties of this essential oil.

References

- [1] Febriyanti, R. M., Ramadhania, Z. M., Tjitraresmi, A., Indradi, R. B., Maisyarah, I. T., Maundu, P. M., Muhaimin, M., & Sujarwo, W. (2026). A systematic review of ethnobotanical study in IndonesiaL diversity and cultural patterns of medicinal plant use. *Journal of Ethnobiology and Ethnomedicine*, 22(42), 1-15.
- [2] Rahman, C.S., Santosa, D., & Purwanto. (2022). Aktivitas rimpang temulawak sebagai antibakteri berdasarkan lokasi tumbuhnya: *Narrative Review. Jurnal Pharmascience*, 9(2), 327-343.
- [3] Kapelle, I. B. D., Souhoka, F. A., & Walla, A. M. (2022). Chemical Composition Oil and Ethanol Extract of Nutmeg Leaf and Antibacterial Test Against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. *Indonesian Journal of Chemical Research*, 10(1), 19-26.

- [4] Ndandarmana, N., Tan, T., Sarungallo, A. S., & Ningsi, R. (2025). Germination of Nutmeg Seeds (*Myristica argentea* Warb.) in Various Media with Scarification Treatment. *Jurnal Ilmu-Ilmu Pertanian Indonesia*, 27(1), 47-52.
- [5] Karmanah, Susanto, S., Widodo, W. D., & Santosa, E. (2020). The Fruit Characteristics of Ambon Forest Nutmeg (*Myristica fatua* Houtt) and Banda Nutmeg (*Myristica fragrans* Houtt). *JUPI*, 25(2), 291-298.
- [6] Ha, M. T., Vu, N. K., Tran, T. H., Kim, J. A., Woo, M. H., & Min, B. S. (2020). Phytochemical and pharmacological properties of *Myristica fragrans* Houtt.: an updated review. *Archives of Pharmacol Research*, 43(11), 1067-1092.
- [7] Khamnuan, S., Phrutivorapongkul, A., Pitchakarn, P., Buacheen, P., Karinchai, J., Chittasupho, C., Takuathung, M. N., Theansungnoen, T., Thongkhao, K., & Intharuksa, A. (2023). The Identification and Cytotoxic Evaluation of Nutmeg (*Myristica fragrans* Houtt.) and Its Substituents. *Foods*, 12(4211), 1-23.
- [8] Orabi, M., Abdulsattar, J. O., & Nasi, Z. O. (2021). Phytochemical profile, antimicrobial, antioxidant activity and Cyclooxygenase 2 inhibitory properties of nutmeg (*Myristica fragrans*) seeds extract. *Egyptian Journal of Chemistry*, 65, 317-326.
- [9] Saputri, A., Fajriah, S., & Cahyana, A. H. (2025). Phytochemical and Pharmacological Properties of *Myristica fragrans* Leaves Houtt. *Alchemy Jurnal Penelitian Kimia*, 21(1), 17-32.
- [10] Ashokkumar, K., Simal-Gandara, J., Murugan, M., Dhanya, M. K., & Pandian, A. (2022). Nutmeg (*Myristica fragrans* Houtt.) essential oil: A review on its composition, biological, and pharmacological activities. *Phytotherapy Research*, 36(7), 2839-2851.
- [11] Devi, N. P. (2025). Pharmacological insights into *Myristica fragrans* (Nutmeg): A systematic review on the therapeutic applications and bioactive compounds. *Plant Science Today*, 11(sp2), 01-11.
- [12] Ullagaddi, R. (2025). The aromatic cure: A scientific review of Nutmeg's medicinal properties. *International Journal of Science and Research Archive*, 15(1), 1656-1663.
- [13] Al-Rawi, S., Ibrahim, A. H., Ahmed, H. J., & Khudhur, Z. O. (2024). Therapeutic, and pharmacological prospects of nutmeg seed: A comprehensive review for novel drug potential insights. *Saudi Pharmaceutical Journal*, 32(6), 1-26.
- [14] Maryati. (2023). Isolation, Characterization, and Identification of Chemical Compounds from Papuan Nutmeg Essential Oil (*Myristica argentea* Warb.). *Gorontalo Agriculture Technology Journal*, 6(2), 65-73.
- [15] Azrial, F. (2025). Potential of bioactive compounds in Indonesian endemic Nutmeg (*Myristica fragrans* and *Myristica argentea*) and their applications in health: An overview. *Journal of Evidence-based Nursing and Public Health (JEVNAH)*, 2(2), 121-137.
- [16] Khamnuan, S., Intharuksa, A., Phrutivorapongkul, A., Theansungnoen, T., Chaichit, S., Thongkhao, K., Samutrtai, P., & Sawangrat, K. (2026). Comparative GC-MS fingerprint analysis of *M. fragrans* and *M. argentea* essential oils: Identifying potential markers for safety and quality control of nutmeg. *Food Chemistry: X*, 33(103395), 1-13.
- [17] Yeuyanan, M. G., Astuti, R. A., & Muslihin, A. M. (2025). Anti-Inflammatory Activity Test of Ointment Preparations of Nutmeg Leaf Extract from Fak-Fak (*Myristica argentea* Warb) Against Burns in Male Wistar White Rats. *Jurnal Eduhealth*, 16(2), 849-856.
- [18] Megawati, M., Darmawan, A., & Hudiyo, S. (2024). Medicinal properties, phytochemistry, and pharmacology of Myristicaceae family: A review. *Journal of Applied Pharmaceutical Science*, 14(05), 038-058.
- [19] Jahajha, A., & Abu-Lafi, S. (2025). Comparative GC-MS profiling of wild *Calamintha incana* leaf essential oils: influence of geographical origin on chemical composition. *Pharmacy & Pharmacology International Journal*, 13(3), 71-75.

-
- [20] Putri, M. K., & Dellima, B. R. E. M. (2022). The Influence of The Area Where It Is Grown on The Caffeine Content of Robusta Coffee Beans (*Coffea canephora*). *Jurnal Ilmu Kesehatan Bhakti Setya Medika*, 7(1), 33-42.
- [21] Mayasari, D., Murti, Y. B., Pratiwi, S. U. T., Sudarsono, S., Hanna, G., & Hamann, M. T. (2022). TLC-Based Fingerprinting Analysis of the Geographical Variation of *Melastoma malabathricum* in Inland and Archipelago Regions: A Rapid and Easy-to-Use Tool for Field Metabolomics Studies. *Journal of Natural Products*, 85(1), 292-300.
- [22] Bont, Z., Züst, T., Arce, C. C. M., Huber, M., & Erb, M. (2020). Heritable variation in root secondary metabolites is associated with recent climate. *Journal of Ecology*, 108, 2611-2624.
- [23] Wang, Y., Liu, H., Yu, S., Zhang, Y., Huang, Y., He, X., & Chen, W. (2024). Effects of geographical, soil and climatic factors on the two marker secondary metabolites contents in the roots of *Rubia cordifolia* L. *Frontiers in Plant Science*, 15(1419392), 01-13.
- [24] Liambila, R. N., Baleba, S. B. S., Wesonga, J. M., Ngamau, C. N., & Wallyambilla, W. (2021). Seasonal and Regional Chemical Variability of the Wild Population of *Lantana camara* Leaf Essential Oil From Kenya. *Journal of Agricultural Sciences*, 13(11), 86-104.
- [25] Shen, Y., Du, H., Liu, F., Gou, X., Tao, Y., Lan, X., Zhang, J., Yin, Y., Li, Q., & Fan, G. (2026). Quality control of herbal medicine based on analytical techniques and machine learning: current advances and future perspectives. *Phytochemical analysis*, 37(4), 488-506.
- [26] Frolova, N., Orlova, A., Popova, V., Bilova, T., & Frolov, A. (2025). Gas Chromatography–Mass Spectrometry (GC-MS) in the Plant Metabolomics Toolbox: Sample Preparation and Instrumental Analysis. *Biomolecules*, 16(1), 16.
- [27] Mwangi, J. M., Kiragu, D., & Chaka, B. (2024). Phytochemical screening, FTIR and GCMS analysis of *Cucurbita pepo* seeds cultivated in Kiambu county, Kenya. *Heliyon*, 10(e30237), 1-10.
- [28] Rao, T. R., Harshitha, S., & Lahari, K. L. (2023). Gas Chromatography-Mass Spectroscopy: An Overview. *European Journal of Biomedical and Pharmaceutical Sciences*, 10(5), 83-89.
- [29] Manurung, H., Susanto, D., Kusumawati, E., Aryani, R., Nugroho, R. A., Kusuma, R., Rahmawati, Z., & Sari, R. D. (2022). Phytochemical, GC-MS analysis and antioxidant activities of leaf methanolic extract of *Lai* (*Durio kutejensis*), the endemic plant of Kalimantan, Indonesia. *Biodiversitas*, 23(11), 5566-5573.
- [30] Nuriah, S., Putri, M. D., Rahayu, S., Advait, C. V., Nurfadhila, L., & Utami, M. R. (2023). Qualitative Analysis of Paracetamol Compounds in Biological Samples Using Gas Chromatography - Mass Spectrometry (GC-MS) Method. *Journal of Pharmaceutical and Sciences*, 6(2), 795-803.
- [31] Abd-ElGawad, A. M., Elshamy, A. I., Al-Rowaily, S. L., & El-Amier, Y. A. 2019. Habitat affects the chemical profile, allelopathy, and antioxidant properties of essential oils and phenolic enriched extracts of the invasive plant *Heliotropium curassavicum*. *Plants*, 8(11), 482.
- [32] Wang, Z., Xiao, S., Wang, Y., Liu, J., Ma, H., Wang, Y., Tian, Y., & Hou, W. 2020. Effects of light irradiation on essential oil biosynthesis in the medicinal plant *Asarum heterotropoides* Fr. Schmidt var. *mandshuricum* (Maxim) Kitag. *PLoS One*, 15(9), e0237952.
- [33] Thamer, F. H., & Thamer, N. (2023). Gas chromatography – Mass spectrometry (GC-MS) profiling reveals newly described bioactive compounds in *Citrullus colocynthis* (L.) seeds oil extracts. *Heliyon*, 9(e16861), 1-9.
- [34] Golian, M., Tančinová, D., Lakatošová, J., Mrvová, M., Gao, J., & Borsányi, P. (2025). Effect of altitude on biomass production and essential oil composition of selected medicinal plants. *Industrial Crops and Products*, 233(121475), 1-18.
-

-
- [35] Sandeep, I. S., Sahoo, B. C., Singh, S., Sahoo, S., Nayak, S., & Kar, B. (2021). Environmental Factors Influencing Yield and Quality of Essential Oils in *Curcuma longa* cv. Lakadong. *Proceedings of the National Academy of Sciences, India Section B: Biological Sciences*, 91, 761-767.
- [36] Abdelmohsen, U. R., & Elmaidomy, A. H. (2025). Exploring the therapeutic potential of essential oils: a review of composition and influencing factors. *Frontiers in Natural Products*, 4, 01-22.
- [37] Wong, X. K., Alasalvar, C., Bo, S., Pan, J., & Chang, S. K. 2025. Unlocking the power of nutmeg: Nutritional composition, phytochemicals, and health benefits revealed through chemometrics and multi-omics advances. *Food Research International*, 218(116798), 1-12.
- [38] Warsito, M. F. (2021). A Review on Chemical Composition, Bioactivity, and Toxicity of *Myristica fragrans* Houtt. Essential Oil. *Indonesian Journal of Pharmacy*, 3(1), 304-313.
- [39] Elfia, H. Y., & Susilo, S. (2023). An update on the pharmacology, phytochemistry, and toxicity of *Myristica fragrans* Houtt. as a source of treatment: A scoping review. *Journal of Applied Pharmaceutical Science*, 13(10): 096-106.
- [40] Quintans, J. S. S., Shanmugam, S., Heimfarth, L., Araújo, A. A. S., Almeida, J. R. G. S., Picot, L., & Quintans-Júnior, L. J. (2019). Monoterpenes modulation cytokines - A review. *Food and Chemical Toxicology*, 123, 233-257.
- [41] Sharma, S., Gupta, J., Prabhakar, P. K., Gupta, P., Solanki, P., & Rajput, A. (2019). Phytochemical Repurposing of Natural Molecule: Sabinene for Identification of Novel Therapeutic Benefits Using In Silico and In Vitro Approaches. *Assay and Drug Development Technologies*, 17(8), 339-351.
- [42] Götz, M. E., Sachse, B., Schäfer, B., & Eisenreich, A. (2022). Myristicin and Elemicin: Potentially Toxic Alkenylbenzenes in Food. *Foods*, 11, 1-26.
- [43] IARC. (2024). Report of the Advisory Group to Recommend Priorities for the IARC Monographs during 2025-2029. *IARC Monographs on the Identification of Carcinogenic Hazards to Humans*. International Agency for Research on Cancer, WHO: France, pp. 1-590.
- [44] IFRA. (2023). *IFRA Standards Documentation: Safrole, Isosafrole and Dihydrosafrole*. <https://ifrafragrance.org/initiatives-positions/safe-use-fragrance-science/ifra-standards/ifra-standards-documentation>. Accessed on August 26, 2026.
- [45] Rahimi, K., Zalaghi, M., Shehnizad, E. G., Salari, G., Baghdezfoli, F., & Ebrahimifar, A. (2023). The effects of alpha-pinene on inflammatory responses and oxidative stress in the formalin test. *Brain Research Bulletin*, 203(110774), 1-7.
- [46] Fraternali, D., Genovese, S., & Ricci, D. (2013). Essential oil composition and antimicrobial activity of aerial parts and ripe fruits of *Echinospira spinosa* (Apiaceae) from Italy. *Natural Product Communications*, 8(4), 527-530.
- [47] Seneme, E. F., dos Santos, D. C., Silva, E. M. R., Franco, Y. E. M., & Longato, G. B. (2021). Pharmacological and Therapeutic Potential of Myristicin: A Literature Review. *Molecules*, 26(5914), 1-15.
- [48] SNI. (2006). *Minyak Pala*. Standar Nasional Indonesia 06-2388. Badan Standar Nasional., pp. 6.
- [49] A'Mun, M. (2013). Karakteristik Minyak dan Isolasi Trimiristin Biji Pala Papua (*Myristica argentea*). *Jurnal Littri*, 19(2), 72-77.
- [50] BMKG. (2026). Data Online – Direktorat Data dan Komputasi - BMKG. *Data BMKG Stasiun Klimatologi Maluku dan Stasiun Meteorologi Pattimura*. <https://dataonline.bmkg.go.id/dataonline-home>. Accessed on August 26, 2026.
- [51] Ayal, F. W., Tubalawony, S., & Abrahamsz J. (2013). Analisis Kelayakan Ekowisata Pantai Lawena, Negeri Hutumuri Kota Ambon. *Jurnal TRITON*, 9(2), 99-105.
-

-
- [52] Irwanto, & Marsono, H. D. (2007). Analisis vegetasi untuk pengelolaan Kawasan hutan lindung Pulau Marsegu, Kabupaten Seram Bagian Barat, Provinsi Maluku. *Tesis*. Universitas Gadjah Mada
- [53] Lotfi, K., Hazrati, S., Oraei, M., Faramarzi, A., & Ajali, J. (2024). Phytochemical variations in *Stachys lavandulifolia* populations and the role of ecological and edaphic factors. *Biochemical Systematics and Ecology*, 113(104798), 1-14.
- [54] Martin, E. R., Díaz, I. E. C., Paciencia, M. L. B., Frana, S. A., Marques, M. O. M., de Moraes, D. R., Eberlin, M. N., & Suffredini, I. B. (2019). Amazon climatic factors driving terpene composition of *Iryanthera polyneura* Ducke in terra-firme forest: A statistical approach. *PLoS One*, 14(11), 1-14.
- [55] Zamani, Z., Tamartash, R., Heydari, Q., & Jelodar, Z. J. (2025). Impact of soil factors and climate on phytochemical characteristics of *Stachys lavandulifolis* Vahl. *Chemistry & Biodiversity*, 22(5): e202402352.
- [56] Silva, J. S., Brandão, V. R., Coutinho, S. D. A., Paciencia, M. L. B., Frana, S. A., Díaz, I. E. C., & Suffredini, I. B. (2021). Antifungal activity of the essential oils of *Osteophleum platyspermum* (Myristicaceae) against *Malassezia* spp. And *Candida albicans* influenced by seasonality and climatic factors. *European Journal of Medicinal Plants*, 32(12), 31-45.