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A Literature Review: Antimicrobial Phenolic Compounds in Nutmeg (*Myristica fragrans* Houtt)

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Abstract

In various countries, testing of phenolic compounds in plants is always carried out because these compounds have various health benefits such as antioxidant, anti-inflammatory, and antimicrobial activities. The types of medicinal plants in Indonesia are known to be very diverse where those included in the medicinal plant group reach more than 1000 species, one of which is nutmeg (*Myristica fragrans* Houtt.) Nutmeg (*Myristica fragrans* Houtt.) itself is native to the Maluku Islands, Indonesia. However, besides the Moluccas, nutmeg is also cultivated in several other tropical countries. The main objective of this literature review is to critically examine the antimicrobial properties and identify the specific antimicrobial components of phenolic compounds contained in nutmeg (*Myristica fragrans* Houtt.) The methodology used in this study involved a comprehensive literature review by utilizing reputable academic databases such as Google Scholar, PubMed, and Science Direct related to articles published between 2019 and 2024. The results of this study were obtained through a thorough search process, resulting in eight articles that were considered to meet the established inclusion criteria. A number of articles showed the effectiveness of nutmeg as an antimicrobial because nutmeg contains phenolic compounds that have antibacterial and antifungal properties, which make it effective as an antimicrobial agent. Therefore, with a more comprehensive understanding of the content of phenolic compounds and their mechanism of action, nutmeg can be a further basis for study in the health sector and the pharmaceutical industry.

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INTRODUCTION

Indonesia has a wide variety of medicinal plants. The use of traditional medicine is generally considered safer than modern medicine. This is due to the relatively fewer side effects of traditional medicine compared to modern medicine. There are more than 1,000 types of plants that have medicinal properties, one of which is nutmeg (*Myristica fragrans* Houtt) (Usman et al., 2024). Nutmeg, which is native to Indonesia, grows in the tropics at altitudes above 700 meters above sea level. It thrives in hot and humid temperatures, with rainfall between 2,000 and 3,500 mm per year, and without significant dry periods. Nutmeg is known as a spice plant that has high economic value and many benefits, because every part of the nutmeg plant, including seeds, fruit, and skin, can be utilized in various industries(Nasir & Marwati, 2022).

Nutmeg is a perennial evergreen tree that can grow to a height of 20-25 feet with soft grayish brown bark and spreading branches (Kaawoan et al., 2016). The plant grows well in warm and humid climates, at an altitude of 1,000 m above sea level with rainfall between 150-250 cm (Ashokkumar et al., 2022; Bayani et al., 2023, 2024). Nutmeg is commonly cultivated in the Maluku Islands, especially Ambon and Banda, Manado, West Sumatra, West Java, and Papua (Simanjorang et al., 2020). Nutmeg (*Myristica fragrans* Houtt*)* is known as a spice plant that has economic and multipurpose value because every part of the plant can be utilized in various food, beverage, medicine, perfume and cosmetic industries (Ginting et al., 2018).

The habit of using nutmeg as a seasoning or consuming it in the form of syrups and sweets will have a very good impact on health, considering that this fruit with a fragrant fragrance has many health benefits. The chemical content contained can overcome insomnia, slimy cough, help digestion, relieve muscle spasms and others. Based on research conducted by the National Science and Technology Authority, in its book Guidebook on the proper use of medicinal plants. Nutmeg contains chemical compounds that are beneficial for health. The skin and flesh of nutmeg, for example, contain essential oils and tanning substances. While mace or nutmeg flowers contain essential oils, tanning agents and starch substances. While the seeds are very high in essential oils, saponins, myristicin, elemisi, lipase enzymes, pectin, lemonene and oleanolic acid. Almost all parts of nutmeg contain chemical compounds that are beneficial to health, including being able to help treat colds, insomnia (insomnia disorders), are stomacic (facilitate digestion and increase appetite), carminative (facilitate bowel movements), antiemetic (overcome nausea and vomiting), menstrual pain and rheumatism (Agaus & Agaus, 2019; Fibonacci & Hulyadi, 2018; Hulyadi et al., 2023).

Nutmeg is generally traded in the form of seeds and mace. The flesh of the fruit is yellowish-white in color, contains a watery gummy liquid, tastes astringent and has astringent properties. Therefore, when the fruit is unripe, the nutmeg pulp cannot be consumed directly but must be processed into various food products. The weight of wet nutmeg meat is equal to 823% of the weight of dried nutmeg seeds . Nutmeg flesh, which is the largest part of nutmeg (77.8%), is usually not utilized. One of the utilization of nutmeg meat is to make nutmeg fruit extract beverage products that are rich in benefits. The nutritional values contained in every 100 g of nutmeg meat are calories (42 cal), protein (0.30 g), fat (0.20 g), carbohydrates (10.90 g), calcium (32 mg), phosphorus (24 mg), iron (1.50 mg), vitamin A (29.50 IU), vitamin C (22 mg), and water (88.10 g) (Aulia et al. 2020).

In addition, nutmeg is reported to have a variety of unique pharmacological therapeutic effects, such as anti-inflammatory, antidiabetic, and antidiarrheal activities. The main chemical components in nutmeg include fat, protein, starch, fixed oil, and essential oil containing myristicin (Biswas, 2022).

In addition to being a spice, nutmeg also has potential as an antimicrobial agent in traditional medicine, especially in the Asian region (Usman et al., 2024). A number of studies have revealed the pharmacological potential of nutmeg, especially in antimicrobial activity where the study states that nutmeg extract can inhibit the growth of gram-positive bacteria such as S. aureus and gram-negative bacteria such as Escherichia coli. This antimicrobial activity is thought to be related to the content of phenolic compounds and antioxidants that have potential as antimicrobials (Nurhasanah, 2014).

Although many studies have revealed the benefits of nutmeg in various aspects of health and industry, studies on the specific pharmacological potential of nutmeg extracts as antimicrobial agents are still very limited. The content of phenol compounds in nutmeg is thought to play an important role in antimicrobial activity. Therefore, this literature review aims to further explore the antimicrobial activity of nutmeg pulp extracts, especially related to the presence of phenol

compounds and antioxidants that act as antimicrobial agents. Thus, this literature review is expected to provide a deeper insight into the potential of nutmeg (*Myristica fragrans* Houtt) as an antimicrobial agent. Through a more comprehensive understanding of the content of phenolic compounds and their mechanism of action, this research can also serve as a foundation for further studies in the health sector and pharmaceutical industry.

METHOD

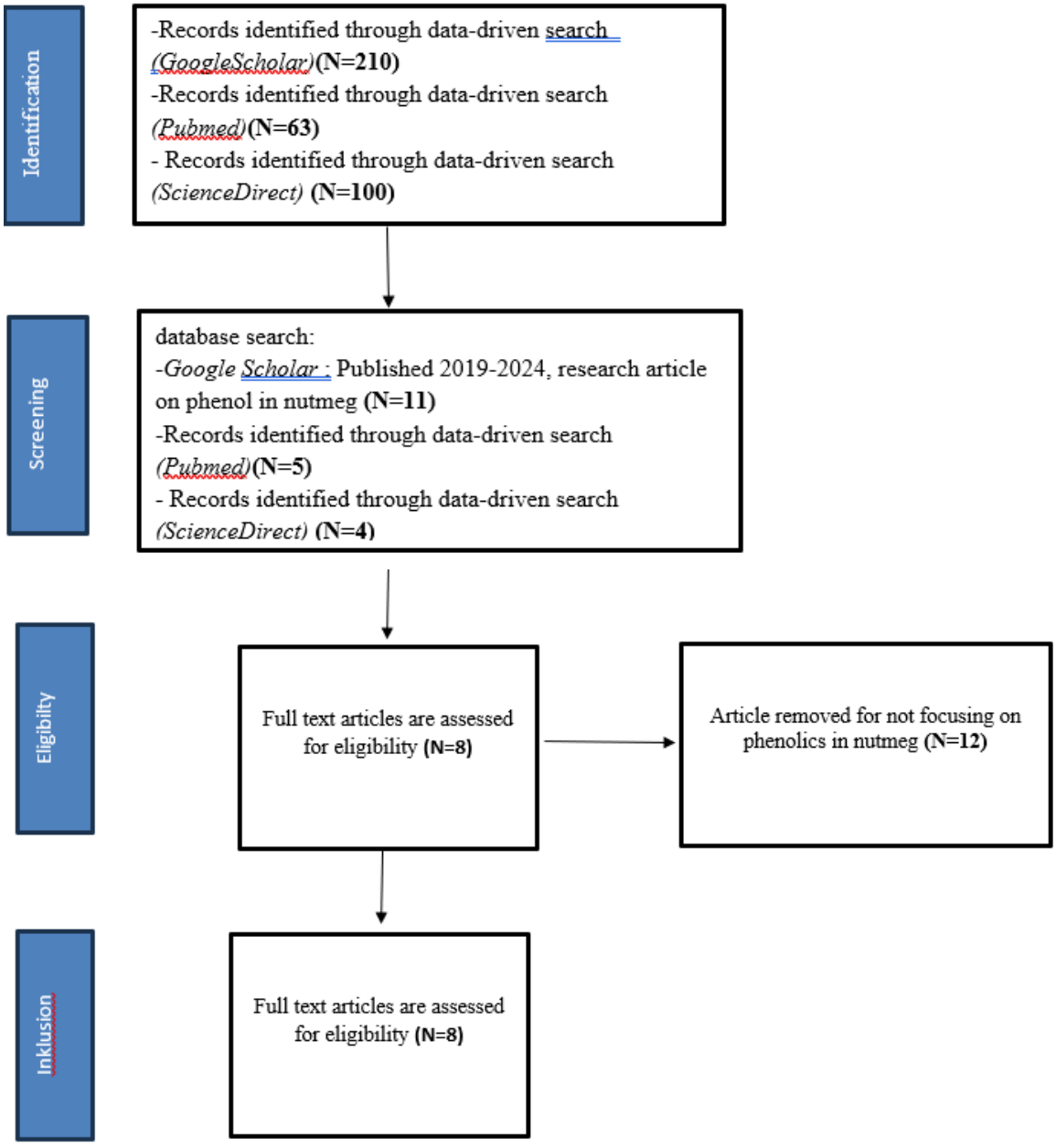

Figure 1: PRISMA Research Flow Diagram

The approach used was an observational study strategy, which involved a comprehensive examination of the existing literature and an in-depth analysis of the potential antimicrobial properties of nutmeg and its components that have antimicrobial effects. Literature review and meta-analysis procedures were conducted based on the guidelines of the preferred reporting items for systematic reviews and meta-analyses (PRISMA)(Arrizqiyani et al., 2018; Fauziyah

& Kuswantoro, n.d.; Handayani et al., 2024; Ismail et al., 2024; Makanaung et al., 2021; Melati Sirait et al., n.d.; Nikolic et al., 2021; Putri Anastasya et al., 2022; Rahman et al., 2022; Rashidian et al., 2022; Rokhmah et al., 2024; S. Aulia, 2020; Suhartini, 2022, 2020; Vakili et al., 2023; Yam, 2024).

Conducting literature searches using Google Scholar, PubMed and Science Direct databases. The search terms entered in the PubMed and Science Direct database queries were "Myristica fragrans Houtt" OR "Phenols in nutmeg, while the search terms used in Google Scholar were 'Nutmeg' OR "(Myristica fragrans Houtt.)" AND "Phenols in nutmeg". From these search results, a total of 20 journals were obtained. However, after applying the inclusion criteria, only 8 journals were considered suitable. The inclusion criteria in this study included full articles, both national and international, written in Indonesian or English, covering the period 2019 to 2024, and focusing on experimental research. In addition, the exclusion criteria included review articles, articles published before 2013, articles that were not in full-text format, and articles that did not contain the specific keyword "Myristica fragrans Houtt".

RESULTS AND DISCUSSION

Several studies have identified different types of phenols in nutmeg, including myristicin, eugenol, and safrole, which have potential as antimicrobials. The activity of these compounds has been tested against various types of pathogenic bacteria such as *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*, as well as fungi such as Candida albicans.

The following that met the inclusion criteria presented various studies related to the antimicrobial activity of phenolic compounds in nutmeg, including the test methods used, the types of microbes tested, and the results obtained are presented in table 1.

Table 1. Search Articles that Meet the Inclusion Criteria

NO	Author(s)	Title	Methods	Result
1	(Trifan et al., 2023)	Article Essential Oils and Sustainability: In Vitro Bioactivity Screening of Myristica fragrans Houtt. Post-Distillation By-Products	Empirical method in which LC-HRMS/MS is used to analyze phenolic compounds.	The results showed that it was rich in phenolic compounds, with total phenolics reaching 63.31 ± 0.72 mg GAE/g. These phenolic compounds, which include flavonoids and phenolic acids, contributed significantly to the antioxidant activity found in the nutmeg waste extract.
2	(Rizwana et al., 2021)	Antifungal, Antibacterial, and Cytotoxic Activities of Silver Nanoparticles Synthesized from Aqueous Extracts	An empirical method in which using the FTIR method reveals the presence of important functional groups such as phenols, alcohols, and carbonyls, which are	That nutmeg (Myristica fragrans) contains phenolic compounds identified through FTIR. These phenolic compounds contribute to the

NO	Author(s)	Title	Methods	Result
		of Mace-Arils of Myristica fragrans	detected through spectral peaks at wavelengths.	bioactive properties of nutmeg,
3	(Shori, 2022)	Storage quality and antioxidant properties of yogurt fortified with polyphenol extract from nutmeg, black pepper, and white pepper	Empirical method in which using the Total Phenolic Content (TPC) of samples in the Folin-Ciocalteu method. Which involves oxidation-reduction reactions between phenolic compounds and Folin-Ciocalteu reagents.	Ferric Reducing Antioxidant Potential (FRAP) value in nutmeg yogurt was the highest ($p < 0.05$).
4	(Blessymol et al., 2024)	An antioxidant study of Titanium dioxide (TiO2) nanoparticles against mace of nutmeg in Myristica fragrans houtt, rhizomes of Curcuma longa linn and Kaempferia galanga extracts	Empirical method in which using FTIR method	The addition of TiO2 synthesis of nutmeg extract occurred the formation of TiO2, which changes the color of the solution from light beige to beige. DPPH antioxidant test shows it has antioxidant activity.
5	(Dareda et al., 2020)	characterization and antioxidant activity of dietary fiber from nutmeg (Myristica fragrans Houtt) pulp	Empirical method in which using FTIR method	the presence of absorption at wave number 3371.57 cm-1 and for nutmeg 3417.86 cm-1 indicates the OH stretch of the hydroxyl group.
6	(Makanaung et al., 2021)	Phytochemical analysis and sedative effect test of ethanol extract and some fractions of nutmeg pulp (Myristica Fragrans Houtt)	Empirical method in which using UV-Vis spectrophotometric method and Sedative effect test	The highest total phytochemical content in nutmeg meat is found in the petroleum ether fraction with a value for total phenolic content of 29.203µg/mL.
7	(Suloi et al., 2023)	Effect of solvent concentration on the chemical content of extracts of fakfak nutmeg (Myristica argentea Warb) pulp	Empirical method in which using Folin-Ciocalteu colorimetric method	Fakfak nutmeg extract has potential as an antioxidant characterized by the presence of phenol content of 12.12 mg/ml at 60% ethanol concentration.
8	(Nomor et al., 2024)	Antioxidant Activity and Determination of	Empirical method where using DPPH (2,2-diphenyl-1-	There were high levels of total flavonoid compounds in the

NO	Author(s)	Title	Methods	Result
		Total Flavonoid Content of Nutmeg Fraction (Myristica fragrans Houtt)	picrylhydrazyl) method and UV-Vis spectrophotometry.	chloroform fraction 142.55 ± 3.83, ethyl acetate fraction 431.89.

The literature search yielded eight publications that met specific inclusion criteria, namely national and international journals containing complete articles, published between 2019 and 2024, and focusing on experimental research. All selected journals have conducted phytochemical analysis of nutmeg (*Myristica fragrans* Houtt.). Specifically, eight publications explored the phenolic compounds in nutmeg (*Myristica fragrans* Houtt.) and their potential as antimicrobial agents.

Research by (Trifan et al., 2023) examined the bioactivity of Myristica fragrans essential oil distillation waste using the LC-HRMS/MS method. The results showed that nutmeg waste is rich in phenolic compounds, with a total phenolic content of 63.31 ± 0.72 mg GAE/g. These phenolic compounds, including flavonoids and phenolic acids, contributed greatly to the antioxidant activity found in the nutmeg waste extract. (Rizwana et al., 2021) examined the antifungal, antibacterial, and cytotoxic activities of silver nanoparticles synthesized using the aqueous extract of nutmeg mace. Using the FTIR method, this study revealed the presence of important functional groups such as phenols, alcohols, and carbonyls detected through spectral peaks at certain wavelengths. The identified phenolic compounds play a role in the bioactive properties of nutmeg.

(Shori, 2022) examined the storage quality and antioxidant properties of yogurt fortified with polyphenolic extracts from nutmeg, black pepper, and white pepper. Using the Folin-Ciocalteu method to measure Total Phenolic Content (TPC), this study showed that yogurt containing nutmeg extract had the highest Ferric Reducing Antioxidant Potential (FRAP) value ($p < 0.05$), indicating strong antioxidant activity. (Blessymol et al., 2024) studied the antioxidant activity of Titanium dioxide (TiO2) nanoparticles against mace extracts of nutmeg, Curcuma longa rhizome, and Kaempferia galanga. Using the FTIR method, this study confirmed the synthesis of TiO2 through changes in the color of the solution from light beige to cream. DPPH antioxidant test showed that the synthesized compound has significant antioxidant activity.

Meanwhile,(Dareda et al., 2020) examined the characterization and antioxidant activity of dietary fiber from nutmeg pulp using the FTIR method. This study found absorption at wave numbers 3371.57 cm^{-1} and 3417.86 cm^{-1}, which indicates the presence of hydroxyl groups (OH). This indicates that dietary fiber from nutmeg has potential as a natural antioxidant. (Makanaung et al., 2021) conducted phytochemical analysis and sedative effect tests of ethanol extracts and several nutmeg meat fractions using UV-Vis spectrophotometric methods. The results showed that the highest phytochemical content was found in the petroleum ether fraction, with a total phenolic content of 29.203 ug/mL, which has the potential to provide sedative effects.

(Suloi et al., 2023) examined the effect of solvent concentration on the chemical content of nutmeg extract from Fakfak (Myristica argentea Warb) using the Folin-Ciocalteu colorimetric method. This study found that Fakfak nutmeg meat extract has potential as an antioxidant, with a phenol content of 12.12 mg/ml at 60% ethanol concentration. (Nomor et al., 2024) examined the antioxidant activity and total flavonoid content of nutmeg meat fractions using the DPPH method and UV-Vis spectrophotometry. The results showed that the chloroform fraction had a total flavonoid content of 142.55 ± 3.83, while the ethyl acetate fraction had a higher flavonoid content of 431.89, indicating high antioxidant potential.

Based on the studies that have been reviewed, phenolic compounds in nutmeg (Myristica fragrans) have great potential as antimicrobial agents. Several studies have shown that phenolic compounds, including flavonoids and phenolic acids, contribute to the bioactive properties of nutmeg, such as antioxidant, antibacterial, and antifungal activities. Research by (Rizwana et al., 2021) confirmed that nutmeg mace extract containing phenolic compounds showed significant antifungal and antibacterial activity through FTIR analysis. This suggests that phenolic compounds in nutmeg have a role in inhibiting the growth of microorganisms. In addition, research by (Trifan et al., 2023) and (Blessymol et al., 2024) also confirmed the presence of phenolic compounds in nutmeg that contribute to antioxidant activity, which can indirectly increase resistance to microbes by counteracting oxidative stress in cells. Furthermore, research by (Makanaung et al., 2021) found that the phenolic content in the petroleum ether fraction of nutmeg pulp is quite high, which could potentially have pharmacological effects, including as antibacterial and antifungal agents.

CONCLUSION

Phenolic compounds in nutmeg have strong potential as natural antimicrobial agents, whether in the form of extracts, nanoparticles, or other synthesized products. These antimicrobial properties are most likely derived from the interaction of phenolic compounds with the microbial cell wall, causing disruption of the microorganism's cell structure and function. However, further research is needed to understand the specific mechanisms and their effectiveness in various pharmaceutical and food applications. The results of the overall literature review indicate that phenolic compounds in nutmeg have potential as promising natural antimicrobial agents Where the main impact of this literature review is the emphasis on the importance of phenolic compounds as active ingredients that can be used in the development of nature-based antimicrobial products where nutmeg containing phenolic compounds also has the potential to replace synthetic chemicals in the control of microorganisms. The main novelty of this literature review lies in the evidence showing that not only extracts, but also nanoparticles and other synthesized forms of phenolic compounds can enhance antimicrobial activity, which may not have previously been widely discussed in the literature. And it is hoped that it can serve as a foundation for further studies in healthcare and the pharmaceutical industry.

RECOMMENDATIONS

This research can still be continued by examining in more detail what affects each method so that the phenolic compounds produced by nutmeg are more optimal.

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