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Isolation of endophytic bacteria from nutmeg plant as antibacterial agents against pathogenic bacteria

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ABSTRACT

Recently, exploration of natural antibiotic alternatives by utilizing medicinal plants is often carried out. Nutmeg plant (*Myristica fragrans* Houtt) is a tropical plant endemic to the Maluku Island and often used as medicine by local people. This study was aimed to isolate endophytic bacteria from the nutmeg plant and detect its potential as an antibacterial against pathogenic bacteria. The study is a descriptive observational study with a true experimental approach. Endophytic bacteria were isolated from several organs of the nutmeg plant such as leaves, leaf bones, stems, fruit flesh, and seeds and then tested for their inhibition against *Staphylococcus aureus, Propionibacterium acne*, and *Escherichia coli*. The results showed that: (1) the highest total population of endophytic bacteria was found in the seeds of nutmeg ($7.5x10^4$ CFU/ml), (2) ten isolates of endophytic bacteria were obtained with varying morphological characteristics, and (3) the detection of antibacterial activity showed that of the 10 isolates obtained, 4 isolates were able to inhibit the growth of *Escherichia coli*, namely isolate BEAD2, BEATD1, BEABJ 2, and BEABJ 1 with the diameter of the inhibition zones of each isolate being 3.4 mm, 3.2 mm, 1.6 mm and 1.5 mm respectively. The conclusion of this study is that 4 isolates of endophytic bacteria were detected as potential antibacterial against *Escherichia coli.*

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INTRODUCTION

Infectious diseases are generally found in developing countries, including Indonesia. Infection occurs when one of the microorganisms that causes infection such as pathogenic bacteria enters the human body and interacts with the host so that it interferes with the body's normal physiology

(Mutsaqof, A.A.N., Wiharto, W., & Suryani, E., 2015). Some of the most common pathogenic bacteria that cause infectious diseases in humans are *Staphylococcus aureus*, *Propionibacterium acne*, and *Escherichia coli* (Kiriwenno et al., 2021; Zahrah et al., 2019; Sumampouw, 2018). The severity of infectious diseases caused by *Staphylococcus aureus* varies so that the mortality and morbidity rates of infection with Staphylococcus aureus are very significant. The results of research conducted by Nuryah et al., (2019) showed that the prevalence of infectious diseases due to Methicilin-Resistant *Staphylococcus aureus* (MRSA) in 2018 was quite high at 12.94%. Furthermore, *Propionibacterium acne* that attacks facial skin has a prevalence rate of 40-80% in the Southeast Asian Region (Zahrah et al., 2019). In addition, *Escherichia coli* which is often associated with the cause of diarrhea and urinary tract infections (Sumampouw, 2018; Seta et al., 2015) has a mortality rate ranging from 17.5%-21% with 1.5 million people suffer from diarrhea every year (Mardianti et al., 2019).

Infections are generally treated with antibiotics. Antibiotics are chemical compounds that function to inhibit or kill the growth of pathogenic microorganisms (Nuryah et al., 2019). The use of antibiotics will be beneficial if they are consumed according to a prescription (Yunita et al., 2021). However, the current relatively high and irrational intensity of use of antibiotics can cause various problems for human health because most of the commercial antibiotics used are synthetic antibiotics that are prone to triggering bacterial resistance. This certainly reduces the effectiveness of antibiotics which in turn becomes a serious global threat and needs to be addressed immediately (Yarza et al., 2015; Yunita et al., 2021). Therefore, efforts to explore natural antibacterials using medicinal plants continue to be carried out, one of which is nutmeg (*Myristica fragrans* Houtt).

In addition to be used as a cooking spice, the nutmeg (*M. fragrans*) also has many health benefits (Agaus & Agaus, 2019). Various studies on the antibacterial activity of nutmeg peel extract (Gansareng et al., 2018), nutmeg leaf and flesh extract (Arrizqiyani et al., 2018), and nutmeg seed extract (Rumopa et al., (2016) have been carried out and reported to inhibit growth of *E. coli*, *S. aureus*, *P. acne* , and *S. pyogenes*. However, not many scientific publications have been recorded regarding endophytic bacteria associated with nutmeg plants and their potential as antibacterial agents. In fact, endophytic bacteria are known to have the same potential with their host plants in producing bioactive compounds because endophytic bacteria live in plant tissues and are able to form a colony without having negative effects on the host (Iqlima et al., 2017). Several studies have reported antibacterial activity produced by endophytic bacteria, such as endophytic bacteria isolated from the Sensaat plant (*Melastoma malabathricum* L.) which were known to be able to inhibit the growth of *Escherichia coli* and *Staphylococcus aureus* (Harahap et al., 2018). Furthermore, endophytic bacteria isolated from the stem of the Yakon plant (*Smallanthus sonchifolius*) had antibacterial activity against *Salmonella typhimurium* (Iqima et al., 2017). In addition to antibacterial, endophytic bacteria also have the ability as antifungals (Yunita et al., 2016). The purpose of this study was to obtain isolates of endophytic bacteria as antibacterial against several pathogenic bacteria that cause infectious diseases.

RESEARCH METHODS

Research Design

This research is a descriptive-observative laboratory research with a true experimental approach using Disk Paper Diffusion Method of Kirby Bauer. The study was intended to obtain and test endophytic bacteria isolated from Nutmeg (*Myristica fragrans* Houtt) as antibacterial against pathogenic bacteria (*Staphylococcus aureus, Propionibacterium acne*, and *Escherichia coli*).

Population and Samples

Nutmeg plant (*Myristica fragrans* Houtt) was sampled using the Purposive Random Sampling method in Kusu-Kusu Hamlet, Ambon. Prior to sampling, every organ of the nutmeg

plant should be ensured that it is old and not infected with fungi.The samples used were mature leaves, leaf bones, stems, seeds, and flesh of nutmeg in fresh condition using sterile plant shears. Fresh plant samples were cleaned of adhering impurities and surface sterilization was carried out.

Procedures

Isolation of Endophytic Bacteria and Total Plate Count Analysis

Plant samples were cut with a size of 1-3 cm. The sample was then immersed in 70% ethanol for 1 minute and immersed in 5.25% sodium hypochlorite solution for 5 minutes, and washed with alcohol 3 times for 30 seconds. Furthermore, the sample pieces were rinsed with distilled water 3 times and dried using sterile tissue. The sample pieces were then chopped and ground using a mortar and serial dilutions were prepared using NaCl. Next, the sample solution was inoculated on Nutrient Agar containing nystatin using the spread plate method and incubated at room temperature. The bacterial colonies that grew were then counted by Total Plate Count (TPC) analysis using a colony counter.

Selection and Characterization of Endophytic Bacteria

Bacterial colonies grown on Nutrient Agar (NA) media were purified to obtain pure isolates. Furthermore, 10 pure isolates that looked different were characterized macroscopically based on colony color, colony shape, colony margin, colony elevation, colony consistency, and colony growth rate.

Inhibitory Test of Endophytic Bacteria Against Several Pathogenic Bacteria

Pathogenic bacterial isolates were scratched/swabbed completely on NA media, while selected endophytic bacterial isolates were spotted on the left and right sides of the media with equal distances and incubated at 30°C for 3 days. The inhibition zone formed was measured using a ruler to determine the vertical diameter and horizontal diameter in mm.

Data Analysis

Data processing was carried out by tabulation and data analysis was carried out descriptively-qualitatively by observing the diameter of the inhibition zone formed by endophytic bacterial isolate against pathogenic bacteria.

RESULT

The results showed that the total population of endophytic bacteria isolated from each organ of the nutmeg plant was quite varied. According to the Total Plate Count (TPC) analysis, nutmeg seeds had the highest total population of endophytic bacteria of $3.0x10^4$ CFU/ml compared to other plant organs (Table 1).

Table 1. Total population of endophytic bacteria isolated from nutmeg (*M. fragrans* Houtt)

No.	Isolate Source	TPC
1	Leaf	4.6×10^3 CFU/ml
2	Leaf Bone	4.1×10^3CFU/ml
3	Stem	2.8×10^4CFU/ml
4	Fruit Flesh	3.0×10^4 CFU/ml
5	Seed	7.5×10^4 CFU/ml

Based on the purification results, 10 isolates of endophytic bacteria were selected which appeared to have different morphologies (Table 2).

Table 2. Purification results of endophytic bacteria isolated from nutmeg plant

Source of Isolate	Number of Isolates	Code of Isolate
Leaf	2	BEAD1 dan BEAD2
Leaf Bone	2	BEATD1 dan BEATD2
Stem	2	BEAB1 dan BEAB2
Fruit Flesh	2	BEADB1 dan BEADB2
Seed	2	BEABJ1 danBEABJ2

Macroscopic characterization showed that endophytic bacteria had various morphology for colony shape, colony elevation, colony margin, colony color and growth rate (Table 3).

Table 3. Colony morphology of endophytic bacteria from nutmeg (*M. fragrans* Houtt)

No	Code of Isolate	Colony Shape	Colony Elevation	Colony Margin	Colony Color	Growth Speed
1	BEAD1	Irregular	Raised	Serrate	Milky White	Moderate
2	BEAD2	Irregular	Umbonate	Lobate	Milky White	Low
3	BEABJ1	Irregular	Raised	Entire	Greenish Yellow	Fast
4	BEABJ2	Irreguler	Convex	Serrate	Greenish Yellow	Fast
5	BEADB1	Circular	Raised	Serrate	Milky White	Moderate
6	BEADB2	Circular	Flat	Lobate	Milky White	Moderate
7	BEATD1	Irregular	Raised	Entire	Milky White	Low
8	BEATD2	Irregular	Flat	Undulate	yellowish white	Low
9	BEAB1	Irregular	Raised	Entire	Beige	Low
10	BEAB2	Irregular	Raised	Lobate	Beige	Low

The results of inhibitory test of 10 isolates of endophytic bacteria isolated from the nutmeg plant (*M. fragrans* Houtt) against pathogenic bacteria (*Staphylococcus aureus, Escherichia coli*, and *Propionibacterium acne*) refers to the clear zone formed around the endophytic bacterial colonies (Figure 4) .

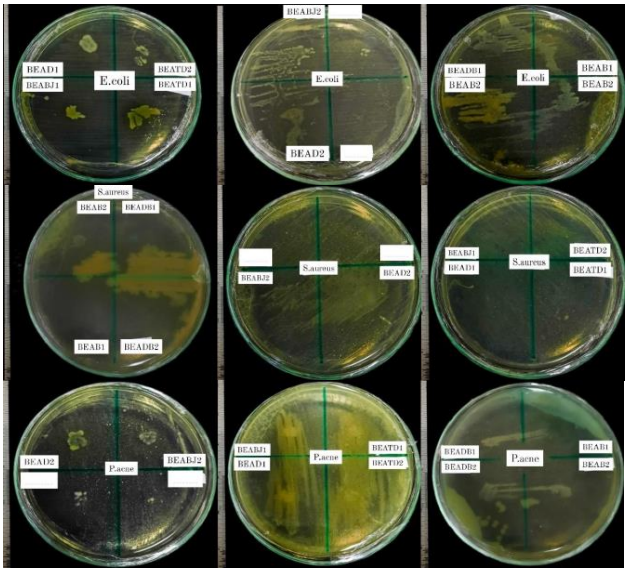

Figure 1. Inhibition zones produced by endophytic bacterial isolates against *Escherichia coli, Staphylococcus aureus, and Propionibacterium acne*

A total of 4 isolates of endophytic bacteria, namely BEABJ1, BEABJ2, BEATD1, and BEAD2 showed the inhibition zones for *Escherichia coli* growth, but did not show an inhibition zone for the growth of *Staphylococcus aureus* and *Propionibacterium acne*. While the other six isolates (BEATD2, BEAD1, BEADB1, BEADB2 , BEAB1, and BEAB2) did not show any inhibition zones at all (Table 4).

Table 4. Diameter of inhibition zone formed by endophytic bacteria against pathogenic bacteria

Endophytic Bacterial Isolate	Inhibition Zone		
	S. aureus	*E. coli*	*P. acne*
BEABJ1	-	1.5 mm	-
BEABJ2	-	1.6 mm	-
BEATD1	-	3.4 mm	-
BEATD2	-	-	-
BEAD1	-	-	-
BEAD2	-	3.2 mm	-
BEADB1	-	-	-
BEADB2	-	-	-
BEAB 1	-	-	-
BEAB2	-	-	-

DISCUSSION

The results of the isolation of endophytic bacteria in this study showed that endophytic bacteria grew in association with all organs of the nutmeg plant (*Myristica fragrans* Houtt). Purwanto et al., (2017) reported that endophytic bacteria are abundant in plant roots because in general the entry route for endophytic bacteria is through the bottom of the plant. However, endophytic bacteria can also enter the upper part of plants that are directly exposed to the air such as flowers, stems, fruits, leaf cotyledons, seeds, and even leaf bones. According to the results obtained, the endophytic bacterial isolates from the nutmeg plant showed the highest total population in the seeds at $7.5x10^4$ CFU/ml, followed by fruit flesh of $3.0x10^4$ CFU/ml, stems of $2.8x10^4$ CFU/ml, leaves of $4.6x10^3$ CFU/ml, and leaf bones of $4.1x10^3$CFU/ml. In contrast to results obtained by Marsaoli et al., (2019) which reported that the population of endophytic bacteria from plant stem tissue is usually higher than that of other organs such as flowers, fruits and seeds. However, it is still possible that the total population of endophytic bacteria in other organs is more than in the stem.

The total population of endophytic bacteria differs from one plant to another. Research conducted by Reppi et al., (2016) on *Catharanthus roseus* plant showed that the highest population of endophytic bacteria was found in plant roots. While the finding results obtained by Mubarokhah et al., (2020) reported that the highest total population of endophytic bacteria isolated from the papaya plant was found in the leaves. Interestingly, each endophytic bacterial strain has its own ability to determine its habitat, thus the total population of endophytic bacteria in each plant organ is different. This depends on the type of plant, plant species, plant age, plant genotype, plant tissue type, research methods and techniques used, geographical conditions of the environment, surface sterilization process, and culture medium used (Marsaoli et al., 2019)

According to the results of this study, the number of endophytic bacterial isolates obtained from the nutmeg plant (*Myristica fragrans* Houtt) was 10 isolates with the composition: 2 isolates from seeds, 2 isolates from leaves, 2 isolates from leaf bones, and 2 isolates from meat. fruit. The selection of isolates was based on differences in colony morphology on media in petri dishes. It can be said that the data is quite valuable considering that there are not many empirical data reporting

findings regarding the comparison of the number of isolates of endophytic bacteria isolated from various organs of the nutmeg plant.

The morphological characterization of endophytic bacteria obtained refers to Bergey's Manual of Determinative Bacteriology. Characterization of endophytic bacterial isolates showed different characteristics and had their own characteristics. The morphological characteristics of endophytic bacteria included the colony shapes, namely circular and irregular. Colony margins included lobate, serrate, entire, and undulate. Colony colors obtained were milky white, yellowish white, greenish yellow, and beige. Colony elevations include flat, raised, covex, and umbonate. Growth rates include slow, moderate, and fast (Table 3). These results are in accordance with research conducted by Irdawati et al. (2017) that obtained various macroscopic characteristics of endophytic bacteria from bay leaves (*Syzygium polyanthum*). Likewise, the morphology of endophytic bacteria isolated from bangle (*Zingiber cassumunar*) is also different from each other and has its own peculiarities (Aglinia et al. 2020). According to the findings obtained by Bhore and Sathisha (2010), endophytic bacteria in plant tissue consist of several genera and species so that they have different characteristics when grown on culture media.

The results of the inhibition test of endophytic bacteria isolated from nutmeg (*Myristica fragrans* Houtt) against the growth of several endophytic bacteria (*Sthapylococcus aureus, Escherichia coli*, and *Propionibacterium acne*) showed that only 4 isolates were able to inhibit the growth of *E. coli* but did not inhibit *S. aureus* and *P. acne*, while the other six endophytic bacteria did not show inhibition zones against the three pathogenic bacteria (Table 4). The diameter of the clear zone produced by the four isolates ranged from 1.5 mm-3.4 mm. The difference in the diameter of the clear zone is caused by differences in bacterial species and the ability of these isolates to produce secondary metabolites that have antibacterial activity (Kusumawati et al. 2014).

The appearance of a clear zone around the endophytic bacterial colonies indicated that endophytic bacteria from the nutmeg plant (*Myristica fragrans* Houtt) were detected to have antibacterial activity against pathogenic bacteria, particularly *Escherichia coli*. This is reinforced by research conducted by Kusumawati et al. (2014) which showed that endophytic bacteria from the Miana plant (*Coleus scutellariodes*) were able to inhibit the growth of *E. coli*. In addition, the leaves, seeds and flesh of nutmeg are often used by local people as medicine and the extracts have been studied by Gansareng et al. (2018) and Arrizqiyani et al. (2018) and the results showed an inhibitory activity against *E. coli* because it was known to contain phenols, terpenoids, and flavonoids. This confirms that endophytic bacteria have the ability to synthesize bioactive compounds that tend to be the same as their host plants (Iqlima et al. 2017). While research on nutmeg leaf bones has never been conducted, it is possible that endophytic bacteria from leaf bones also have potential as a new antibacterial source. The association of endophytic bacterial isolates with plants is a form of mutually beneficial interaction because the nutrients needed by endophytic bacteria are obtained from plant metabolism, while endophytic bacteria provide protection for plants from pathogenic bacteria attack (Purwanto et al. 2017).

CONCLUSION

Isolation of endophytic bacteria from nutmeg plant (*Myristica fragrans* Houtt) succeeded in obtaining 10 isolates of endophytic bacteria, with 4 isolates of which (isolate BEATD1, BEAD2, BEABJ1, BEABJ2) were detected to have the potential to be used as antibacterial agents against pathogenic bacteria, particulary *Escherichia coli*.

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