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Review Article

Traditional Uses and Pharmacology Study of *Piper betle L*: A Systematic Review

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ABSTRACT

Betel leaf (*Piper betle L.*) is a plant that has been widely used for medicinal purposes. Parts of the betel plant, such as the roots, seeds, and leaves, have potential for medicinal use, but the leaves are most commonly used. Empirically, betel leaves have been used by the community as an antibacterial agent. There are many studies and research that have reported the antibacterial activity of betel leaves. Its diverse bioactive compounds, such as flavonoids, phenols, and essential oils, provide a broad pharmacological potential. This study aims to identify the pharmacological effects of betel leaves based on a systematic literature review (PRISMA). Literature searches were conducted through scientific databases such as Google Scholar using relevant keywords. Thirty articles selected were published within a certain period and met the inclusion criteria. The results of the review showed that betel leaves have various pharmacological activities, including antibacterial, antifungal, antioxidant, anti-inflammatory, and analgesic. Flavonoids and phenols play an important role in antioxidant and anti-inflammatory activities, while essential oils contribute to antimicrobial activity. This literature review highlights that green betel leaf (*Piper betle L.*) possesses significant pharmacological effects, including antimicrobial, antioxidant, anti-inflammatory activities, and other therapeutic potentials, making it a promising natural candidate for herbal medicine development.

Keywords:
Piper betle L.; Pharmacology; Antibacterial; Bioactive Compounds; Literature Review.

INTRODUCTION

Indonesia is a country rich in herbal plants, one of the herbal plants that are widely recognized by the public as herbal plants is green betel leaf (*Piper betle L.*). Green betel leaf is one of 13 types of plants that have the highest antibacterial activity. Green betel leaf (*Piper betle L*) contains essential oil in which there is phenol content which is one of the antibacterial substances. The phenol content contained in green betel leaves (*Piper betle L.*) is more than phenol in general (Kusuma et al., 2017). Green betel leaves (*Piper betle L.*) have long been recognized in the traditional medicine of various cultures. This vine has a long history of use in the traditional medicine systems of Southeast Asia, including Indonesia. Its diverse phytochemical compounds, such as flavonoids, phenols, and volatile oils, provide interesting pharmacological potential for further study. Interest in the pharmacological potential of green betel leaf is increasing along with the development of science. Modern research has revealed a variety of biological activities from this plant, including antibacterial, antioxidant, anti-inflammatory, analgesic, and anticancer. The content of various bioactive compounds in green betel leaves is the basis of these pharmacological activities. A number of studies have been conducted to reveal the mechanism of action and potential application of green betel leaves in the pharmaceutical field. Previous studies have

successfully isolated and identified various active compounds from green betel leaves and tested their effectiveness against various types of diseases. However, further research is still needed to deeply understand the mechanism of action of these compounds and develop safe and effective drug formulations based on green betel leaves.

The part of the green betel plant that is often utilized is the leaf. Green betel leaves are flat shaped like a heart, have a leaf color on the surface that is green and smooth. Green betel leaves have a leaf width of 3.5-10 cm and a leaf length of 5.5-18 cm. Betel leaves grow intermittently, pointed, and aromatic. Betel leaves are believed to contain antiseptic substances or antibacterial substances (Emilia Putri et al., 2023). Betel leaves have a distinctive aroma because they contain 1-4.2% essential oil, water, protein, fat, carbohydrates, calcium, phosphorus, vitamins A, B, C, iodine, sugar and starch. Of these various contents, in essential oils there are natural phenols that have antiseptic power 5 times stronger than ordinary phenols (bactericidal and fungicidal) but not sporasid. Essential oil from betel leaves contains 30% phenol and some of its derivatives. The essential oil consists of hydroxy cavicol, cavibetol, estragol, eugenol, methylugenol, carbacrol, terpenes, sesquiterpenes, phenylpropanes, and tannins, Cavicol is the most abundant component in the essential oil that gives betel leaf its characteristic odor. Kavikol is easily oxidized and can cause discoloration (Annisa et al., 2017).

In recent decades, scientific interest in natural medicinal plants has increased. Green betel leaf, with its empirically proven properties, has become one of the focuses of research. Previous studies have revealed various pharmacological activities of green betel leaf, including as an antioxidant, antibacterial, anti-inflammatory, and analgesic. This potential makes green betel leaf a promising candidate for the development of new medicines.

The pharmacological potential of betel leaf has been demonstrated in various in vitro and in vivo studies. In addition to its strong antimicrobial activity, betel leaf has also shown positive effects in treating various skin diseases, such as acne and eczema, through its anti inflammatory and antibacterial mechanisms. The anticancer potential of betel leaf has also caught the attention of researchers, with several studies demonstrating the ability of betel leaf extracts to inhibit cancer cell growth through apoptotic and cyclotoxic mechanisms. In addition, betel leaf also has potential in managing chronic diseases such as diabetes mellitus, through its hypoglycemic effects.

Several studies have demonstrated the pharmacological benefits of green betel leaves, including as antibacterial, antifungal, and antioxidant agents. Its extract has been shown to be effective in inhibiting the growth of pathogenic bacteria such as *Staphylococcus aureus* and *Escherichia coli,* as well as fungi such as Candida albicans. In the context of antioxidants, the phenol and flavonoid compounds in green betel leaves play an important role in preventing cell damage that can lead to degenerative diseases such as diabetes, cancer, and cardiovascular disorders. The anti-inflammatory activity of betel leaf has also been confirmed through inhibition of the release of inflammatory mediators, which makes it potential in the management of inflammatory diseases. In addition, several studies have shown the anticancer potential of green betel leaves, where eugenol has antiproliferative effects against various cancer cells, such as breast cancer and skin cancer.

Green betel leaf also has traditional benefits that are supported by modern scientific evidence. Traditionally, it is used for the treatment of wounds, mouth ulcers, and minor infections, as well as a natural antiseptic for oral hygiene and the feminine area. Further research shows that the tannins in betel leaves can accelerate tissue regeneration, making them effective in wound healing. On the other hand, the extract is also reported to have hypotensive effects, helping to control blood pressure, and support digestive function.

The use of betel leaf in pharmaceutical products has become increasingly widespread. Betel leaf extract can be found in various preparations, such as mouthwash, ointment, and tablets. However, it should be noted that despite its great potential, the use of betel leaf in the pharmaceutical field still faces several challenges, such as standardization of extract quality, possible side effects, and interactions with other drugs. Therefore, further research is still needed to optimize the use of betel leaf as a medicinal ingredient.

Although the benefits of betel leaf have been widely documented, further research is still needed to understand its pharmacological mechanisms in depth, determine safe and effective therapeutic doses, and identify potential side effects. In addition, biotechnology-based approaches can be used to increase the efficiency of extracting bioactive compounds from green betel leaves, so that their use in the pharmaceutical world is optimized. With its extensive benefits and potential, green betel leaf is one of the promising medicinal plants for the development of natural material-based therapies.

Various research results on green betel leaf (*Piper betle L.*) show that this plant has a variety of significant pharmacological effects. Research on the antibacterial activity of green betel leaf revealed that the extract was effective against various pathogenic bacteria, such as Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa. In addition, studies have also proven that green betel leaves have good antifungal capabilities, specifically against Candida albicans and Aspergillus niger, making them potential agents for the treatment of fungal infections.

The purpose of this study is to analyze and review various scientific literatures that discuss the pharmacological effects of green betel leaves (*Piper betle L.*), focusing on the potential bioactive compounds contained therein. This research aims to provide a comprehensive understanding of the pharmacological benefits of this plant, such as its antibacterial, antifungal, antioxidant, anti-inflammatory, anticancer activities, as well as its role in wound healing and management of other health conditions. Through this literature review, it is expected to identify the mechanism of action of active compounds such as phenols, flavonoids, tannins, eugenol, and essential oils in providing therapeutic effects.

METHODS

The method used for writing this article is based on data collection from online journals published during the last 15 years, 2009-2024. Sources were obtained from international and national journals. A systematic search was conducted using the Google Scholar database, which yielded a total of 5,310 articles and other databases 4,260 articles published between 2016 and 2024. To ensure comprehensive coverage, keyword combinations used: "green betel leaf (*Piper betle L.*)", "pharmacological effects of green betel plant (*Piper betle L.*)", "activity test of green betel plant (*Piper betle L.*)". In addition, the search was limited to articles within the focus area of health and pharmacological effects experiments.

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework was adopted to guide the article selection process. The process involved three main stages such as identification, screening, eligibility, and inclusion. Relevant keywords were identified by consulting previous studies, thesaurus, and expert recommendations.

Table 1. Inclusion and Exclusion Criteria

Criteria	Inclusion	Exclusion
Language	Indonesian and English	Other than Indonesian and English
Type paper	Journal Article	Literature review, an overview, narrative review
Experiment Method	Health, biology, chemistry medical science, pharmacy	Agriculture, psychology, energy, social sciences, farming

Inclusion and exclusion criteria used in the selection of research literature. In the inclusion column, articles were considered that were in Indonesian and English, had a journal article format, and used experimental methods in the fields of health, biology, chemistry, medical science, or pharmacy. Conversely, in the exclusion column, articles that were not considered were those that used languages other than Indonesian and English, belonged to literature types such as literature review, an overview, or narrative review, as well as articles that discussed topics outside the scope of the specified experimental methods, such as agriculture, psychology, energy, social sciences, and agriculture. These criteria aimed to ensure the relevance and quality of the articles in supporting the research focus.

Based on the inclusion and exclusion criteria provided in Table 1, a total of 56 articles were deemed eligible for further review. These criteria pertained to article type (journal articles), language (Indonesian and English), and field of study (health sciences, biology, chemistry, and medical sciences). Full text access was obtained for 56 potentially relevant articles. After further review, 26 articles were eliminated due to closed access, lack of relevance to the inclusion categories, and the remaining 30 articles were further reviewed and identified as suitable for further in-depth analysis.

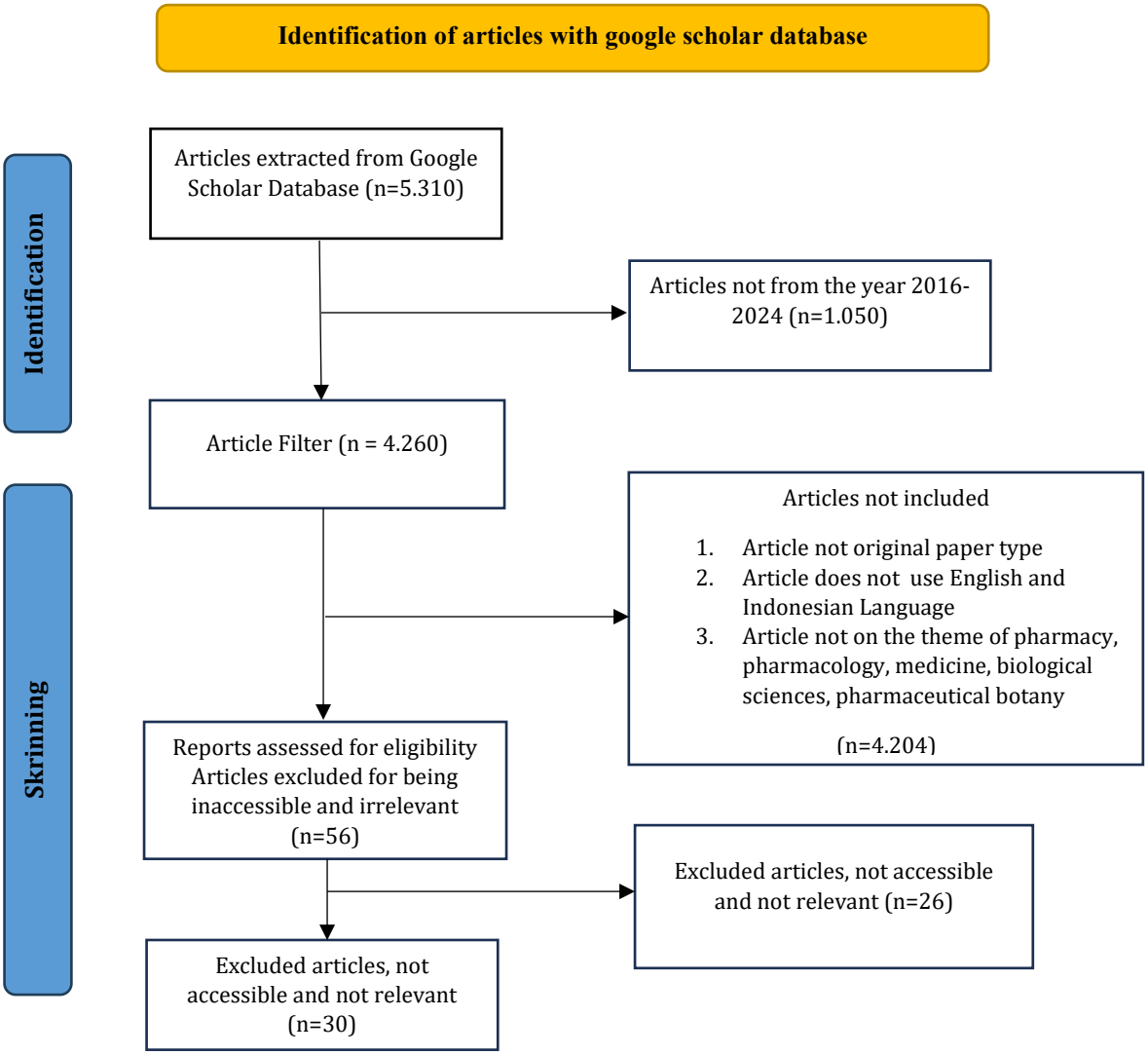

Figure 1. literature selection process

RESULTS AND DISCUSSION

This section presents the analysis of the 30 selected articles, with grouping results such as solvents, sample parts, test animals, extraction methods, and pharmacological effects (summarized in Tables and Diagrams).

Table 2. Table of Selected Article Analysis

No	Author	Solvent	Sample Part	Test Animal / Microorganism	Extraction Method	Pharmacological Effect
1	Aprillia & Safitri, 2020	96% Ethanol	Leaf	Mice	Maceration	Antidiabetic, Antibacterial
2	Dewi et al., 2021	Copper acetate 5%	Leaf	None	Maceration	Antibacterial
3	Kusuma et al., 2017	Aquadest	Leaf	*Streptococcus agalactiae*	Percolation	Antibacterial

No	Author	Solvent	Sample Part	Test Animal / Microorganism	Extraction Method	Pharmacological Effect
4	Deru et al., 2019	Water	Leaf	*Mangrove crab (Scylla serrata)*	Maceration	Antibacterial
5	Selfyana & Musdalipah, 2018	Water	Leaf	*Candida albicans*	Maceration	Antifungal
6	Zulfikri & Dianti, 2022	70% Ethanol	Leaf	*Staphylococcus aureus/escherich ia coli*	Maceration	Antiseptic
7	Jeffrey & Sugiaman, 2023	Ethanol, methanol, water	Leaf	*Streptococcus mutans*	Maceration	Antibacterial, Antiinflammatory, Antidiuretic, Antiseptic, Antioxidant, Antimicrobial, Digestive
8	Sukatin et al., 2022	Distilled water, Ethanol 96%, and Water	Leaf	None	Maceration	Not specific
9	Hayyudiah et al., 2024	Methanol, ethyl acetate, ethanol, water, n hexane	Leaf	*Salmonella typhimurium, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa*	Extraction	Antibacterial
10	Emilia Putri et al., 2023	70% Ethanol	Leaf	*Pathogenic bacteria, fungi*	Maceration, Percolation	Antiseptic
11	Sadiah et al., 2022	Water and Ethanol	Leaf	*Taphylococcus aureus, Escherichia coli, Bacillus subtilis, Salmonella typhi, Pseudomonas aeruginosa, Klebsiella pneumoniae*	maceration, infusion, reflux, extraction with different solvents	Antibacterial, Antiinflammatory, Antifungal, Antioxidant, Antidiabetic.
12	Daswito et al., 2019	Ethanol	Leaf extract	*housefly (musca domestica)*	Maceration	Unspecific
13	Arina et al., 2023	96% ethanol	Leaf	*Staphylococcus aureus*	Maceration	Antibacterial, Antiinflammatory, Antiseptic, Immunomodulator
14	Rasmiati et al., 2022	Glycerin, peppermint oil	Leaf	*Streptococcus mutans, Escherichia coli, staphylococcus aureus*	None	Antiseptic and Antibacterial, Antibacterial, Antifungal, Antioxidant
15	Ni Luh Putu Taksayani Putri & Ni Luh Putu Vidya	Methanol, ethanol, aquadest	Leaf extract	*Bacillus subtilis, staphylococcus aureus, Escherichia coli*	Diffusion, microdilution methods	Antibacterial, Antiinflammatory, Antioxidant, Antiseptic

No	Author	Solvent	Sample Part	Test Animal / Microorganism	Extraction Method	Pharmacological Effect
	Paramita, 2023					
16	Haryanti et al., 2020	70% Ethanol	Leaf	Not specific	Maceration	Antibacterial
17	Dewi et al., 2019	Methanol	Leaf	*Propionibacterium acnes, Malassezia furfur yeast*	Maceration	Antimicrobial, Antiinflammatory, Antioxidant
18	Zahara & Pamekas, 2023	Sterile distilled water and NaOCl 2 solution 10%	Leaf	*Pyricularia oryzae*	Maceration	Antifungal, Antimicrobial, Antidiuretic
19	Hafid et al., 2019	Ethyl acetate	Leaf	*Staphylococcus aureus, escherichia coli, mosquito larvae*	Maceration	Antimicrobial
20	Buana Januarti et al., 2023	Methanol	Leaf	*Male rabbit Staphylococcus aureus, Escherichia coli*	Maceration	Antimicrobial, Antioxidant
21	Christiani et al., 2023	Ethanol, methanol, distilled water	Leaf	None	Distillation water-vapor	Antioxidant
22	Lestari et al., 2023	96% ethanol and dimethylsulfoxide (DMSO)	Leaf	Male white mice *(Mus musculus)*	Maceration	Analgesic, Antibacterial, Antidiuretic, Antiinflammatory, Antioxidant
23	Rasydy et al., 2019	96% Ethanol	Leaf	*Staphylococcus aureus*	Maceration	Antiseptic, Antimicrobial
24	Rahmawati, 2021	Water	Leaf	Green locust	Maceration	Antibacterial, Antiinflammatory, Antifungal
25	Oktavia et al., 2017	70% Ethanol	Leaf	Male white mice *(Mus musculus)*	Maceration	Antidiuretic, Antibacterial, Hepatoprotective, Antioxidant, Antiinflammatory
26	Annisa et al., 2017	Methanol	Leaf	Rabbit	Maceration	Antiseptic
27	Fitriani et al., 2024	DMSO 10% and distilled water	Leaf	*Candida albicans*	Steam distillation	Antifungal
28	Talcha Pertiwi et al., 2021	Ethanol	Leaf	None	Maceration	Antiinflammatory
29	Ummah, 2019	Ethanol	Leaf	Stophylociccus	Maceration	Antibacterial
30	Sikumbang et al., 2022	Ethanol	Leaf	Mice	Maceration	Antiinflammatory

Solvent Profile

Based on the diagram attached in Figure 2, presents comparative data on the use of various types of solvents in a process or experiment conducted. Ethanol with a percentage of 16.67% as the most commonly chosen solvent, followed by DMSO and water. The use of other solvents such as methanol, aquadest, 96% ethanol, and 70% ethanol is also quite significant, indicating flexibility in solvent selection based on the characteristics of the compounds to be dissolved or the purpose of the experiment. This considerable variation in solvent use indicates that solvent selection is a crucial step in a study. Factors such as solvent polarity, compound solubility, and experimental objectives significantly influence the choice of appropriate solvent. For a more in-depth analysis, it is necessary to consider the specific context of the experiments performed, such as the type of compound being studied and the objectives to be achieved.

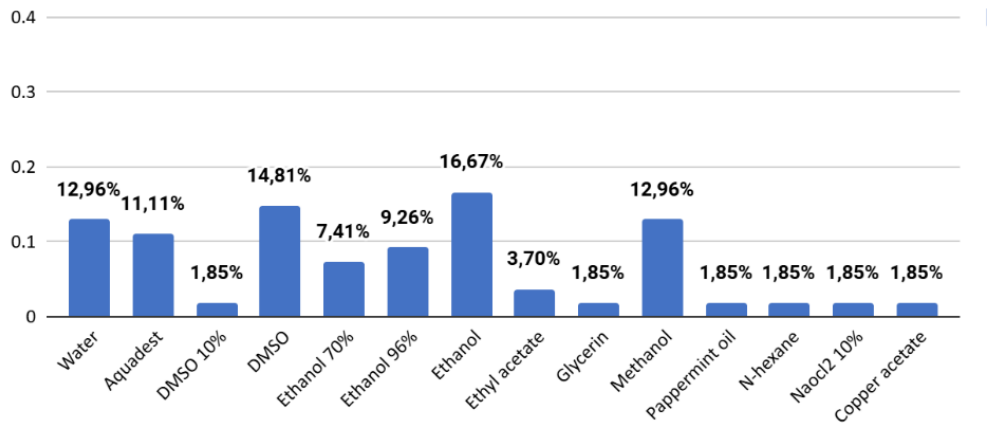

Figure 2. Diagram of the percentage of solvent used

In the context of the literature study of the pharmacological effects of green betel leaf, the use of ethanol and methanol as solvents supports the isolation and characterization of bioactive compounds with high efficiency, thereby increasing the validity of the research results. According to research by Hakim & Saputri (2020), green betel leaves (*Piper betle L.*) are macerated using ethanol solvent. The reason for using this solvent is because ethanol is a polar solvent so that it is able to attract antibacterial compounds such as phenols, tannins and flavonoids where these compounds are polar compounds. Another reason is because the solvent is easily available, efficient and safe for the environment. In addition, research by DLY Handoyo (2020), said that in general, methanol and ethanol solvents are the most widely used solvents in the maceration process because of their large polarity distribution.

According to DLY Handoyo (2020), solvent selection is based on the ability of large polarity or semipolar so that it can dissolve various chemical components in polar to nonpolar samples in maximum quantities. The principle of extraction is based on the distribution or distribution of solutes in active compounds with the use of a ratio of two solvents that do not mix with each other or different polarity properties.

Profile of the Plant Part Utilized

Based on the diagram attached in Figure 3, it shows that most of this research focuses on the use of green betel leaves in whole form. With a percentage of 93.3%, whole green betel leaves were the main component in this experiment. The relatively small use of green betel leaf extracts, only about 6.7%, indicates that this study is more interested in the potential benefits of green betel leaves as a whole, including compounds that may not be fully extracted

Figure 3. Diagram of the percentage of sample used

Green betel leaf (*Piper betle L.*) is known to contain a variety of phytochemical compounds that play an important role in its pharmacological activity, including flavonoids, tannins, saponins, alkaloids, essential oils, and phenols. These compounds have potential as antimicrobial agents, antioxidants, anti-inflammatory, as well as other therapeutic activities that support the use of green betel leaves as herbal medicinal materials.

Research conducted by Sahara (2020), states that green betel leaf (*Piper betle L.*) is a traditional medicinal plant that is closely related to oral health. Green betel leaves contain phenolic propanoid compounds, tannins, and essential oils containing betelfenol, cavicol, estragol, eugenol, and carvacol. These compounds have strong antibacterial and antifungal properties and can inhibit the growth of various types of bacteria.

Profile of Test Animals or Microbes

Based on the diagram attached in Figure 4, presents data on the percentage of the use of various types of animals or test microbes in research or experiments conducted. The categories observed include bacteria, fungi, other microorganisms, as well as the status of no test organisms ("None"). From the diagram, it can be seen that Staphylococcus aureus is the most commonly used microbe, with the highest percentage reaching 19.57%. Furthermore, Escherichia coli and Mouse also have a significant proportion, at 15.22% and 8.70% respectively. This varied use of microbes or test animals likely reflects the research need for a particular species, which depends on the purpose of the experiment, such as testing for effectiveness, toxicity or other biological characteristics. These data show the distribution of the proportion of different types of organisms that are relevant in a particular field of research.

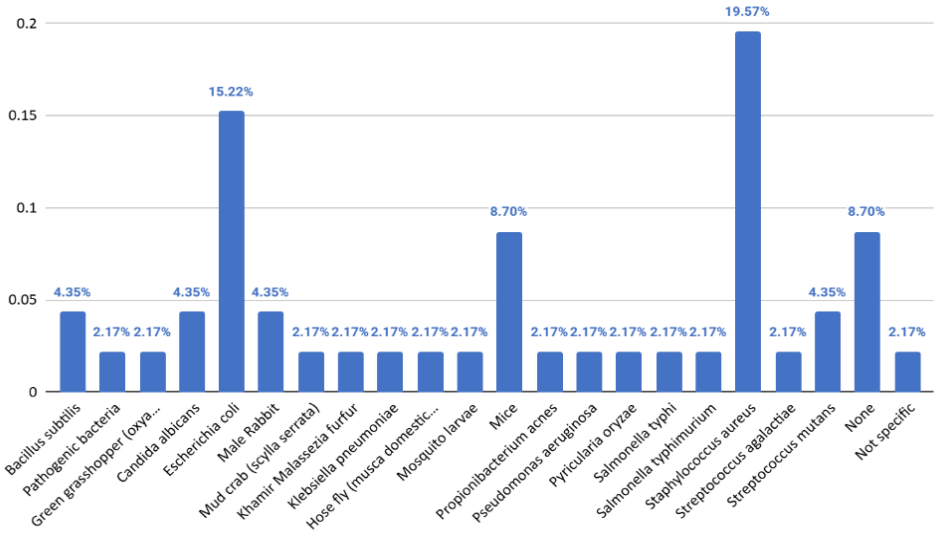

Figure 4. Diagram of animal/microbe test percentage

Many studies have been conducted to test the effectiveness of betel leaf extract against E.coli and S.aureus. Several studies have shown that green betel leaf extract has a sizable zone of inhibition against these two types of bacteria, indicating its potential as an antimicrobial. According to (AR Utami 2013), these two bacteria have the ability to develop resistance to various antibiotics. Research using E. coli and S. aureus in test animals allows evaluation of the effectiveness of new antibiotics and alternative treatment strategies.

The use of test animals in scientific research plays an important role in the development of science, especially in the fields of biomedicine and pharmacology. According to (Intan & Khairi, 2020), said that the selection of laboratory animals must be in accordance with the research objectives and characteristics of the disease or function under study. The animals used must meet certain criteria to be suitable for the function or disease that is the object of research.

Profile Of Extraction Method

Based on the diagram attached in Figure 5, it shows that the maceration method dominates as the most frequently used extraction method, with a percentage of 64.86%. This shows that maceration is the main method of choice in this study. In addition to maceration, other extraction methods such as diffusion, steam distillation, extraction, infusion, microdilution, percolation, and reflux were also used, but with smaller and relatively equal percentages. The use of these diverse methods indicates that the study tried various approaches to extract the desired compounds. There is also a "none" category which indicates that in some cases, samples may not have gone through the extraction process. This can happen if the sample is already in extract form or if the purpose of the study does not require extraction

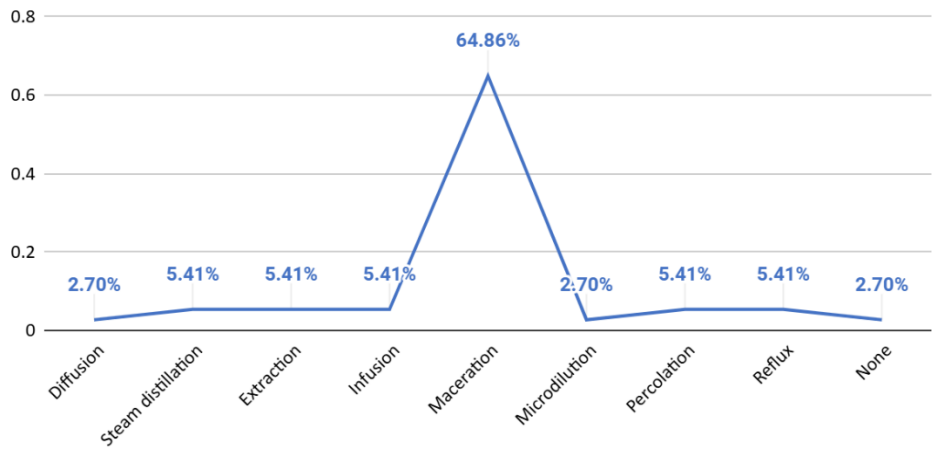

Figure 5. Diagram of Extraction Method Profile

Betel leaf contains various bioactive compounds such as essential oils, flavonoids, tannins and alkaloids. Many of these compounds are sensitive to high heat. In maceration extraction, no excessive heating is required, so that easily degradable or volatile compounds such as essential oils can be well preserved. For example, research by Rukayadi et al. (2013) showed that extraction with ethanol solvent through maceration was able to extract bioactive compounds from green betel without damaging the chemical structure of easily degradable compounds.

The extraction method used is highly dependent on the type of compound to be extracted, the nature of the plant material, and factors such as cost, time, and efficiency. Modern technologies such as ultrasonic, supercritical fluid extraction, and microwave assisted extraction offer many advantages, such as time efficiency, reduced solvent use, and higher extract quality. However, high equipment and energy costs can be an obstacle. On the other hand, traditional methods such as maceration, percolation, and steam distillation remain in use due to their ease, low cost, and better scalability in many applications. For example, Sari et al. (2018) showed that although maceration can produce extracts with good active compound content, the efficiency of time and solvents used is still a major concern.

Profile of Pharmacological Effects

Based on the diagram attached in figure 6, it presents the percentage of studies that focus on the various pharmacological effects of a compound or a drug certain extracts. Pharmacological effects refer to the influence of a substance on bodily functions. Antibacterial effects were the main focus in most studies, with the percentage reaching 22.4%. This shows that many studies were interested in the potential of compounds or extracts as antimicrobial agents. In addition to antibacterial effects, studies also investigated a variety of other pharmacological effects, such as analgesic (pain relief), anti-inflammatory (inflammation), antioxidant, and immunomodulatory. These effects indicate the potential of the compound or extract in the treatment of various diseases. There is an "unspecified" category which indicates that some studies may not have specifically identified the pharmacological effects of the compounds or extracts studied.

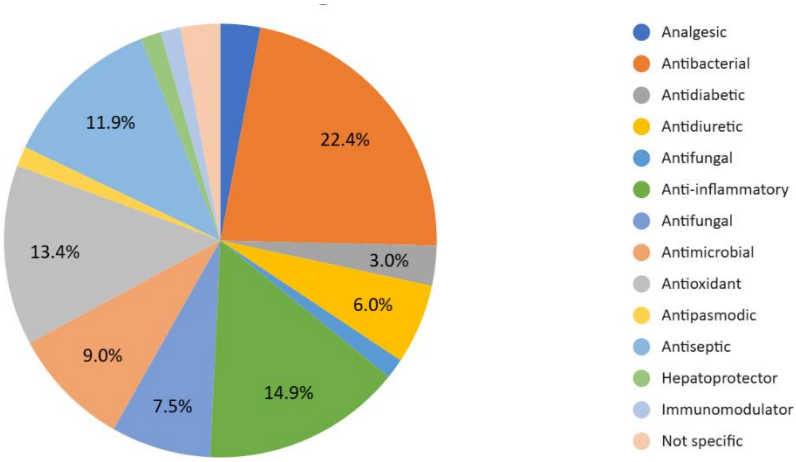

Figure 6. Pharmacological Effects

Green betel leaf (*Piper betle L.*) has been recognized in various studies as a plant with significant antibacterial potential. According to Syah et al. (2008), active compounds in green betel leaves, such as phenols, flavonoids, and essential oils, are known to have antimicrobial effects against various types of pathogenic bacteria. Phenolic compounds, in particular, have the ability to disrupt bacterial cell membranes, thus slowing or even stopping bacterial growth. In addition, flavonoids contained in green betel leaves can also act as antioxidant agents that inhibit the activity of important enzymes in bacterial metabolism, which contributes to the antibacterial activity of these leaves. Another study by Khanna et al. (2012) also showed that green betel leaf extract effectively inhibited the growth of pathogenic bacteria such as Staphylococcus aureus and Escherichia coli, two bacteria often associated with human infections.

In addition to phenolic compounds and flavonoids, essential oils contained in green betel leaves also have strong antibacterial potential. Chaudhury et al. (2017) stated that green betel leaf essential oil, which contains components such as eugenol and cavicol, has antimicrobial properties that can kill or inhibit the growth of pathogenic bacteria. Eugenol, in particular, is known to have a disinfecting effect and can damage bacterial cell walls, causing leakage of cellular components that ultimately lead to bacterial death. This antibacterial activity makes green betel leaves one of the potential natural sources for the development of safer and environmentally friendly antibacterial drugs or antiseptic products.

Green betel leaf (*Piper betle L.*) has various pharmacological potentials thanks to the content of active compounds such as eugenol and flavonoids. Research by Khanna et al. (2012) showed that green betel leaves have significant antibacterial activity against Staphylococcus aureus and Escherichia coli, making them effective against bacterial infections. In addition, a study by Ravindra et al. (2010) revealed that green betel leaf extract has a strong anti-inflammatory effect, which can inhibit inflammation

through its effect on the prostaglandin pathway. This suggests that green betel leaf has great potential as a natural therapy for the treatment of infections and inflammatory conditions.

CONCLUSION

An in-depth literature study on the pharmacological effects of green betel leaf (*Piper betle L.*) reveals the great potential of this plant in medicine. Various studies have shown that betel leaves contain active phytochemical compounds such as flavonoids, phenols, and volatile oils that have a variety of biological activities. These activities include antibacterial, antioxidant, anti-inflammatory, analgesic, and antimicrobial. This potential makes betel leaf a promising candidate for the development of natural medicines to treat various diseases, such as bacterial infections, inflammation, and degenerative diseases. However, further research is needed to optimize the use of betel leaf, including the right dosage, effective formulation, and a more detailed mechanism of action. In addition, the long-term safety of betel leaf use also needs to be comprehensively studied before it can be widely applied in clinical practice.

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