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Review

The Potential of Betel Leaf (Piper betle L.) Against Bacteria to Cure Mastitis: A Systematic Review

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Abstract

Introduction: Mastitis is a problem in breastfeeding that causes nutritional deficiencies in the baby. Staphylococcus aureus is one of the bacteria that cause mastitis. Betel leaf (Piper betle L.) has been used in several health problems and has antimicrobial activity. This study aims to explore the potential of betel leaf (Piper betle L.) against bacteria to cure mastitis.
Methods: A systematic review was carried out according to the PRISMA guidelines. Searches were conducted in three databases namely PubMed, Google Scholar, and ScienceDirect. The search uses keywords according to the Mesh term, namely 'betel leaf (Piper betle L.)', 'bacteria', and 'Mastitis'. 198 articles were found in a database search. 15 studies were analyzed.
Results: All studies found that both types of piper betle, both green and red, showed positive effects in the treatment of mastitis. Processing techniques, storage, and certain concentrations such as boiling temperature affect the optimum inhibition zone of bacteria. The addition of certain formulas also increases the antimicrobial activity.
Conclusion: The use of antibiotics and betel leaf extract can be used simultaneously to treat mastitis. Betel leaf (Piper betle L.), has a positive effect on the management of mastitis, but processing techniques, concentrations, and adjuvants need to be studied further.

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INTRODUCTION

Human milk contains all the essential nutrients a baby needs for growth and development, and contains antibodies for their immunity. Exclusive breastfeeding is breast milk given to babies from birth to 6 months without adding or replacing it with other foods or drinks [1]. Globally, there has been an increase in the coverage of exclusive breastfeeding from 38% in 2012 to 44% in 2020 [2]. However, this still does not meet the global target indicator for 2025, which is to increase the rate of exclusive breastfeeding by at least 50% [3].

There are problems in breastfeeding which can cause the baby's milk intake to decrease. Mastitis is one of the problems experienced by breastfeeding mothers. Common complaints during breastfeeding were blocked milk ducts (29%), nipple discharge (23%), swollen breasts (21.2%), breast lumps (19.2%), infections (5.7%), and mastitis (3.8%) [4]. In line with this, about 17% of mothers with mastitis stop breastfeeding [5].

Mastitis can occur at any time but is more common during breastfeeding, [6] with a percentage of 3-20% based on a survey from the Academy of Breastfeeding Medicine [7]. Mastitis is defined as inflammation of the breast with or without infection, caused by static milk and infection from bacteria [8]. In 94.1% of the breast milk samples, it contained at least one bacterial isolate from the genus Staphylococcus [9]. The bacteria that most often causes mastitis is Staphylococcus aureus [10]. Not only in humans, Staphylococcus aureus also infects mammals, goats, and cows [11].

Treatment of mastitis can be done with proper counseling, supportive therapy, symptomatic treatment, and antibiotics in addition to efficiently removing milk. Several studies have reported high rates of prescribing antibiotics for the treatment of mastitis such as penicillin, cephalosporin, erythromycin, or clindamycin as prevention and control measures [9]. However, there is limited consensus regarding the condition of mastitis that should receive antibiotic therapy, the right time to start therapy, duration, and pathology have an impact on the development of bacterial resistance to antibiotics. Therefore, natural materials are increasingly attractive to be used as an alternative to the prevention and treatment of mastitis because of their high effectiveness, few side effects, residues, and low resistance [12].

Betel leaf (Piper betle L.) can be found in the yards of people's houses which are widely used as traditional medicine, food supplements, and daily needs. The use of betel leaves as a traditional medicine is widely practiced, especially in Asia. For example, the habit of chewing betel leaves is believed to be beneficial for preventing bad breath, strengthening teeth gums, and stimulating the digestive system. In addition, in Indonesia it is used to maintain vaginal hygiene, in India and Thailand it is used as a mouthwash, in Malaysia it is used to treat dental problems, headaches, coughs, pain, and arthritis, in Sri Lanka it is used to treat skin diseases [13].

The characteristics of betel leaf can be an opportunity for researchers to develop

various products, especially in the food and pharmaceutical industries. Utilization of betel leaves in producing modern merchandise can improve the economy of local farmers. A systematic review conducted in 2005-2018 reported that to date there have been no studies using betel leaf extract as an alternative anti-inflammatory therapy for mastitis. In addition, more studies have looked at mastitis in mammals than mastitis in humans [13], [14]. Inducing Staphylococcus aureus bacteria in the mammary rats shows typical pathological changes that are similar to the state of mastitis so that it is possible to conduct pre-clinical research on alternative mastitis therapies which can become the basis for the development of human research [15]–[17]. This study aims to explore the potential of betel leaf (Piper betle l.) against bacteria to cure mastitis.

METHODS

Study Design and Search Strategy

A systematic review was conducted to explore the potential of betel leaf (Piper betle L.) against Staphylococcus aureus to cure mastitis. The preparation of the report is following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines [18]. The search was conducted through the PubMed, Google Scholar, and ScienceDirect databases on the 2020-2021 English-language studies using a combination of the following Medical Subject Heading (MeSH) terms and relevant keywords. The keywords used were Piper betle AND Staphylococcus aureus AND Bacteria AND Mastitis. Boolean operators are used in searches using AND, OR, and NOT. The bacteria examined in detail in this study were Staphylococcus aureus, Streptococcus agalactiae, Escherichia Coli, etc.

Study Selection and Outcome Measure

The inclusion criteria applied in the selection of manuscripts were research in English or Indonesian, evaluating the potential of betel leaf (Piper betle L.) against bacteria to cure mastitis, providing full text, and published in 2013-2023. The exclusion criteria for this study were case reports, letters to editors, study reviews, and abstracts without full text.

Data Extraction

The authors performed title and/or abstract screening independently of the included articles using standard Microsoft Excel forms. The formal assessment of article quality was carried out using modified Cochrane EPOC checklist [19].

Data Abstraction and Synthesis

As a first step, relevant results are extracted, sequenced, and examined to identify subthemes and themes. The results of the synthesis were carried out by all authors. Table 1 describes the quality of the study. Table 2 describes the characteristics of the study included.

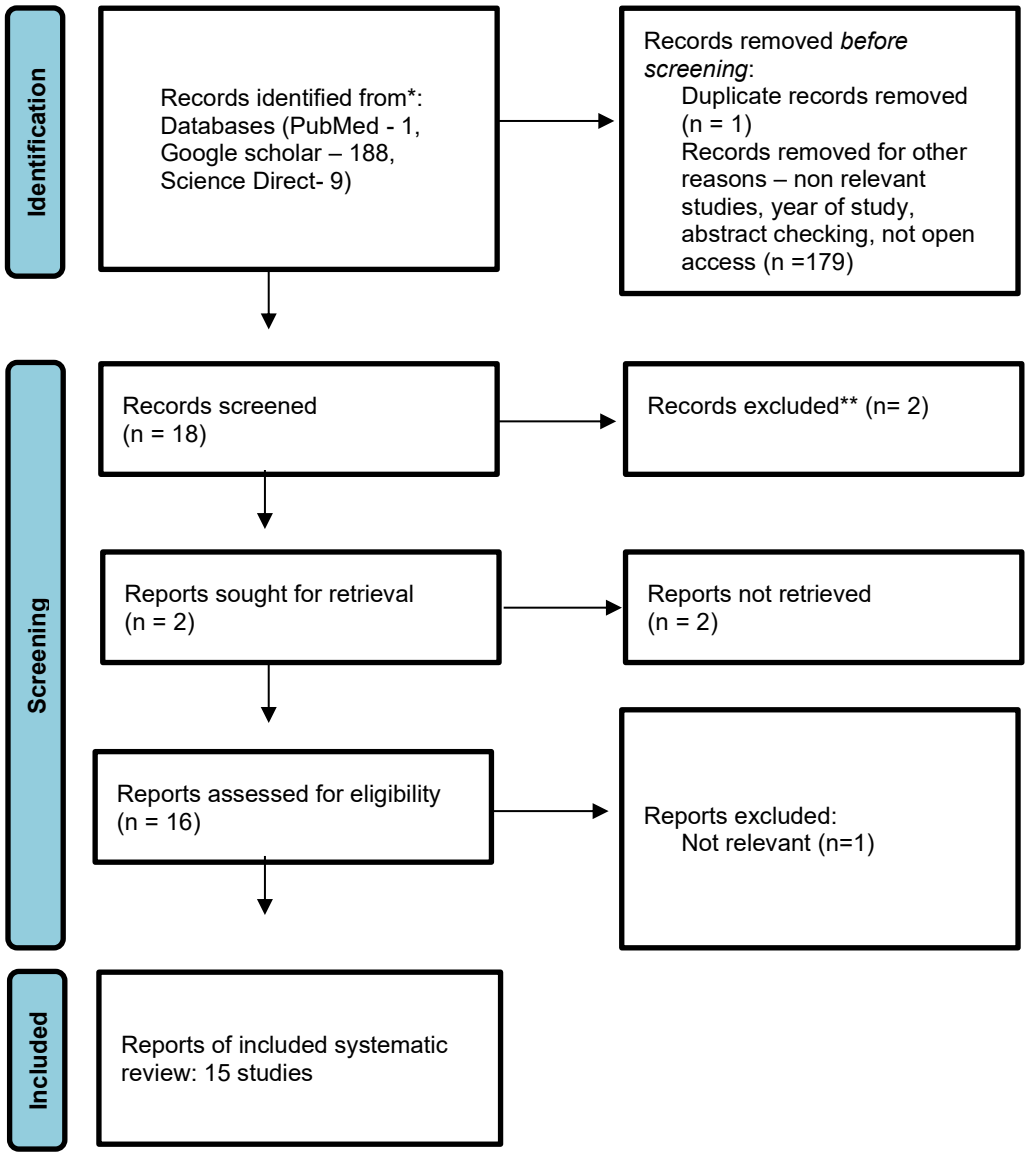

Figure 1. Prisma Flow Research

RESULTS

Search Results and Study Quality

The search results for articles in the three databases found a total of 198 studies. A total of 180 were removed for reasons such as non-relevant studies, year of study, abstract checking, and not open access. A total of 15 articles were screened. Finally, 15 studies were included in the assessment. The results of the quality assessment showed that 15 studies had moderate to low quality.

Samples, Main Ingredients, and Additional Ingredients

Not all studies use breastmilk samples. There were 2 studies using milk samples infected with mastitis. Thirteen other studies have

focused on betel leaf for mastitis cases in livestock. The ingredients used vary, mostly using green betel leaf extract. A total of 1 study used Betel leaf meal (BLM) and Red betel leaves. A total of 4 studies did not use additional materials. The other 4 use additions, namely Napier grass, Roots of Asparagus racemosus, fruits of Terminalia bellirica, torch ginger flower extract, turmeric extract, Curcuma domestica, Curcuma zanthorrhiza, and karbopol.

Bacterial Type

There are 2 studies specifically studying Staphylococcus aureus. Other studies are studying other bacteria such as Streptococcus agalactiae, and Escherichia coli.

Finding

All studies found that both types of piper betle, both green and red, showed a positive effect on treating mastitis, both in the form of extracts and BLM. Certain processing techniques, storage, and concentrations such as boiling temperature affect the optimum inhibition zone and inhibition effect of bacteria. The addition of certain formulas also increases the carrying capacity of piper betle to fight mastitis. In a study, the best herbal antibacterial formulation was a combination of 50% betel leaf extract, 50% torch ginger flower extract, and 50% turmeric extract. Green betel leaf extract (by solvent evaporation) has almost the same ability as 30% iodide. Betel leaf water extract has the same effectiveness as the antibiotic penicillin-dihydrostreptomycin. In addition to antimicrobial activity, two other studies discussed Somatic cell count (SCC), total plate count (TPC), and milk production. The use of piper betle does not change the composition of milk, treats subclinical mastitis in dairy cows, improves the microbiological quality of fresh cow's milk, and increases milk production.

DISCUSSION

All studies found that both types of Piper betle, both green and red, showed a positive effect on treating mastitis, both in the form of extracts and BLM. Chemical compounds present in betel leaves such as essential oils, chavicol, eugenol, flavonoids, saponins, and phenols have roles as antimicrobial, antifungal, antibacterial, antioxidant, and anti-inflammatory. The selection of betel leaf extraction is necessary to ensure efficient phytochemical compounds [14]. Betel leaf extract has great potential as a source of natural therapeutic agents for bacterial infections. Other studies have found that this leaf is useful, especially for conjunctivitis, but betel leaf extract (Piper betle L.) needs further research before it can be used as an alternative therapy [20]. The antibacterial and antifungal properties and safety profile of betel leaf strongly support its application in the development of various products, especially in the food and pharmaceutical industries [13].

Certain processing techniques, storage, and concentrations such as boiling temperature affect the optimum inhibition zone and inhibition effect of bacteria. The most effective method for making betel leaf extract is by maceration with ethanol solvent [21], [22]. Apart from processing, Betel leaves

are easily damaged and decompose quickly, so various preservation techniques are adopted to minimize post-harvest loss of betel leaves [14]. Betel leaf (Piper betle L.) is a commercial plant, which has been traditionally consumed raw as a mouth freshener and stimulant in Southeast Asia since ancient times. It has various functional and medicinal properties, such as antimicrobial, antioxidant, anti-diabetic, anti-carcinogenic, etc. However, some health hazards can occur, if the leaves are consumed together with areca nut and tobacco [23].

The addition of certain formulas also increases the carrying capacity of piper betle to fight mastitis. In a study, the best herbal antibacterial formulation was a combination of 50% betel leaf extract, 50% torch ginger flower extract, and 50% turmeric extract. Research on the activity of betel leaf extract in inhibiting the growth of Staphylococcus Aureus was carried out at various extract concentrations ranging from 2.5% to 75% [24]–[27]. The higher the concentration of betel leaf extract, the stronger it inhibits the growth of Staphylococcus Aureus [28].

Green betel leaf extract (by solvent evaporation) has almost the same ability as 30% iodide. Betel leaf water extract has the same effectiveness as the antibiotic penicillin-dihydrostreptomycin. The combination of betel leaf extract and essential oil with antibiotics (streptomycin, chloramphenicol, and gentamicin) could provide potentiating antibacterial properties [13]. There is a potential synergy that occurs between the use of antibiotics and betel leaf extract [29].

This study could not be meta-analyzed due to different methods. This study also has not explored piper betle in cases of mastitis in humans. All studies lead to animal research. Future research needs to apply the use of betel piper in humans.

CONCLUSION

All studies found that both types of Piper betle, both green and red, showed a positive effect on treating mastitis, both in the form of extracts and Betel leaf meal. Certain processing techniques, storage, and concentrations such as boiling temperature affect the optimum inhibition zone and inhibition effect of bacteria. The addition of certain formulas also increases the carrying capacity of piper betle to fight mastitis. The use of antibiotics and betel leaf extract can be used together to improve the quality of health services.

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