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Review: Antibacterial activity of lime (*Citrus aurantifolia* L.) peel

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ABSTRACT

Over the past three decades, a plethora of scientific publications have indicated that medicinal plants may offer a viable substitute for antibiotics. Research on the antibacterial activity of lime peel, or *Citrus aurantifolia* L., has been widely published. This review aimed to highlight the lime peel as antibacterial agents. Numerous scientific papers included for this review demonstrated the potentially effective antibacterial properties of lime peel. Strong antibacterial activity is exhibited by lime peel essential oils, extracts, and fractions. One component of lime peel essential oils that contributes to its antibacterial properties is limonene. According to this study, infections brought on some bacteria including cariogenic bacteria and acne bacteria can be treated using lime peel.

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INTRODUCTION

Worldwide rates of morbidity and mortality were high due to infectious diseases prior to the turn of the 20th century (Adedeji, 2016). One of the primary methods utilized in modern medicine to treat infections is the use of antibiotics. The 1930s to 1960s were considered the "golden era" of antibiotics, during which time numerous antibiotics were developed. Sadly, this age came to an end since scientists could no longer keep up the rate of antibiotic discovery in the face of microorganisms that were developing resistance. (Aslam et al., 2018). Antibiotic use is extremely prevalent throughout Southeast Asia, especially Indonesia, where it exceeds 80% in a number of regions (Fatimah & Kurniawati, 2024). The overuse and inadvertent application of antibiotics leads to the development of resistance in bacteria (Hasan & Al-Harmoosh, 2020).

Since ancient times, the main source of therapeutic medications has been medicinal plants. Over the past three decades, a plethora of scientific publications have indicated that medicinal plants may offer a viable substitute for antibiotics (Abdallah et al., 2023). Compounds obtained from medicinal plants may offer new, simple strategies for combating pathogenic bacteria.(Vaou et al., 2021). As the problem of antibiotic resistance worsens, plant natural products offer a promising source of antibacterial lead molecules that may be able to help fill the drug development pipeline (Porras et al., 2021). Natural plant compounds with significant potential for application include polyphenols, alkaloids, and tannins. They can be used as antibiotic resistance modifiers or as antimicrobials (Alsheikh et al., 2020). There have also been reports of essential oils' biocidal qualities, particularly their broad range of activity against different bacterial species (Cho et al., 2020).

One type of medicinal plant in the Rutaceae family is the citrus. Citrus fruits are extensively consumed because they contain a variety of bioactive metabolites that are beneficial to the body's health. The portion of orange peel that is typically thrown away has certain properties, such as antibacterial properties (Rafiq et al., 2018). About 40–50% of the fruit component is made up of citrus peel, a byproduct of processing citrus fruit. The peel of the citrus fruit contains the majority of the essential oil (Singh et al., 2021).

Large amounts of *Citrus aurantifolia*, or lime, are found in tropical countries, including Asia (Puspita et al., 2020). Research on the antibacterial activity of lime peel, or *Citrus aurantifolia* L., has been widely published. The antibacterial activity of lime peel includes the antibacterial activity of extracts, fractions and essential oils.

However, despite these gains, there are still areas of knowledge that are lacking in the current body of literature, which require additional research. Although there is evidence supporting the antibacterial effects of citrus peel extracts, further investigation is required to determine the particular mechanisms of action and the effectiveness against clinically relevant bacterial strains. Moreover, there is a need for further exploration in the field of standardised extraction procedures and the identification of bioactive chemicals that are responsible for antibacterial activities. This is necessary in order to effectively apply these discoveries in practical medical and healthcare settings.

The present study seeks to fill these knowledge gaps by specifically investigating the antibacterial properties of lime peel extracts against clinically significant bacterial strains. This study aims to provide significant insights into the current efforts to prevent antibiotic resistance and explore alternative therapeutic options derived from natural sources such as citrus fruits.

The study's background highlights the pressing necessity for new antibacterial drugs in the face of the antibiotic resistance challenge. Exploring natural alternatives to antibiotics shows promise in the use of medicinal plants, namely citrus fruits such as lime. Additional study is necessary to thoroughly analyse the antibacterial attributes of lime peel extracts and apply these discoveries to develop efficient therapies for bacterial illnesses.

RESEARCH METHOD

Acquiring pertinent material on the use of lime peel as an antibacterial agent likely entailed a systematic search and evaluation of papers from academic databases and platforms including Google Scholar, PubMed, Elsevier, and ResearchGate. The publication timeframe, spanning from 2012 to 2022, indicates that the emphasis will be on conducting fresh research to ensure the inclusion of the latest findings.

The researchers likely conducted extensive searches using keywords such as "lime peel," "Citrus aurantifolia," "antibacterial activity," and others to assess the quantity of literature available on the topic. There would have been numerous first search results from this.

Probable procedures carried out throughout the data collection phase include: Keyword Search: Researchers utilized specific keywords in databases like Google Scholar, PubMed, Elsevier, and ResearchGate to locate articles pertaining to the subject. Screening and Selection: After locating the articles, they underwent a screening process based on certain criteria to determine which ones to include and which ones to exclude. During the screening phase, the titles, abstracts, and keywords were reviewed to identify potentially relevant papers.

Full-text assessment: The complete versions of some articles were acquired and assessed based on specific criteria to determine their suitability for inclusion in the study.

Data Extraction: Pertinent information from the included papers was extracted for analysis. The study encompassed objectives, methodologies, findings, and deductions pertaining to the antimicrobial properties of lime peel.

Researchers typically initiate their work by doing comprehensive searches in databases to gather a substantial volume of literature, allowing them to gain a comprehensive understanding of the existing research. However, only a portion of the collected literature would be utilized in the study. Several factors would influence the selection of stories to be included: The authors selected articles for inclusion based on their relevance to the main topic of the review, which is the effectiveness of lime peel as an antibacterial agent.

Emphasis would be placed on incorporating high-quality studies with robust methodologies and transparently providing clear results, prioritizing quality and reliability.

Publication Date: To ensure the evaluation encompasses the latest advancements in the discipline, articles published between 2012 and 2022 will be taken into account.

Scope and Coverage: The ultimate objective is to provide a comprehensive overview of the current knowledge regarding the antibacterial characteristics of lime peel, encompassing various aspects of the subject.

The rationale behind not utilizing all the literature that was collected is to ensure the study's credibility, relevance, and focus. The review's findings and conclusions are more robust when it exclusively incorporates high-quality and pertinent studies. Additionally, selecting the books to be included in the review may provide challenges, such as language hurdles, restricted availability, and publication biases. In order to conduct a comprehensive and valuable assessment of lime peel as an antibacterial agent, it is crucial to select relevant material in a coherent and systematic manner.

RESULTS AND DISCUSSIONS

Antibacterial activity of lime peel using diffusion method

Research on the antibacterial activity of lime peel has been carried out, both by diffusion and dilution methods. Table 1 shows the results of antibacterial activity using the paper disc diffusion method, while table 2 shows the results of antibacterial activity using the well diffusion method.

Table 1. Antibacterial activity of lime peel using agar diffusion (paper disc) method

Microbe	Sample	Concentration	Inhibitory zone (mm)	Reference
Gram-positive bacteria				
Bacillus cereus	Petroleum ether fraction	300 µg/disk	10	(Ghosh et al., 2020)
	Chloroform fraction	300 µg/disk	19	(Ghosh et al., 2020)
	Hydromethanol fraction	300 µg/disk	8	(Ghosh et al., 2020)
B. megaterium	Chloroform fraction	300 µg/disk	14	(Ghosh et al., 2020)
B. subtilis	Petroleum ether fraction	300 µg/disk	9	(Ghosh et al., 2020)
	Chloroform fraction	300 µg/disk	16	(Ghosh et al., 2020)
Sarcina lutea	Petroleum ether fraction	300 µg/disk	7	(Ghosh et al., 2020)
Staphylococcus aureus	Chloroform fraction	300 µg/disk	15	(Ghosh et al., 2020)
	Essential oil- Al Sharqia	5; 10 µl	6.3; 8.1	(Al-Breiki et al., 2018)
	Essential oil- Al	5; 10 µl	5.5; 9.2	(Al-Breiki et al.,

Microbe	Sample	Concentration	Inhibitory zone (mm)	Reference
	Batinah			2018)
	Essential oil-Muscat	5; 10 µl	7.5; 10.2	(Al-Breiki et al., 2018)
Streptococcus mutans	Methanol extract	20; 50%	13.6; 22.1	(Jeffrey et al., 2020)
	n-hexane fraction	2; 10; 20; 50%	10.1; 12.5; 13.6; 18.1	(Jeffrey et al., 2020)
	Ethyl acetate fraction	10; 20; 50%	13; 21; 28.7	(Jeffrey et al., 2020)
	Water fraction	50%	20.8	(Jeffrey et al., 2020)
Gram-negative bacteria				
Salmonella paratyphi	Petroleum ether fraction	300 µg/disk	9	(Ghosh et al., 2020)
	Chloroform fraction	300 µg/disk	15	(Ghosh et al., 2020)
S. typhi	Chloroform fraction	300 µg/disk	13	(Ghosh et al., 2020)
Vibrio parahemolyticus	Chloroform fraction	300 µg/disk	13	(Ghosh et al., 2020)
	Hydromethanol fraction	300 µg/disk	6	(Ghosh et al., 2020)
V. mimicus	Petroleum ether fraction	300 µg/disk	6	(Ghosh et al., 2020)
	Kloroform fraction	300 µg/disk	13	(Ghosh et al., 2020)
	Hydromethanol fraction	300 µg/disk	6	(Ghosh et al., 2020)
Escherichia coli	Petroleum ether fraction	300 µg/disk	9	(Ghosh et al., 2020)
	Chloroform fracion	300 µg/disk	16	(Ghosh et al., 2020)
	Hydromethanol fraction	300 µg/disk	8	(Ghosh et al., 2020)
	Essential oil-Al Sharqia	5; 10 µl	0; 2.2	(Al-Breiki et al., 2018)
	Essential oil-Al Batinah	5;10 µl	0; 3.1	(Al-Breiki et al., 2018)
	Essential oil-Muscat	5; 10 µl	5.8; 8.2	(Al-Breiki et al., 2018)
Shigella dysenteriae	Petroleum ether fraction	300 µg/disk	10	(Ghosh et al., 2020)
	Chloroform fraction	300 µg/disk	15	(Ghosh et al., 2020)
	Hydrometanol fraction	300 µg/disk	8	(Ghosh et al., 2020)
S. boydii	Petroleum ether fraction	300 µg/disk	11	(Ghosh et al., 2020)
	Chloroform fraction	300 µg/disk	13	(Ghosh et al., 2020)
Pseudomonas aeruginosa	Petroleum ether fraction	300 µg/disk	11	(Ghosh et al., 2020)
	Chloroform fraction	300 µg/disk	17	(Ghosh et al., 2020)

Researchers conducted a comparative study to evaluate the efficacy of various lime peel fractions and essential oils against distinct bacterial strains. Chloroform fractions consistently exhibited potent antibacterial activity against several tested microorganisms, such as Bacillus cereus, Staphylococcus aureus, and Escherichia coli. The antibacterial efficacy of essential oils derived from lime peel supplied from different locales varied.

Ghosh et al. (2020) compared the antibacterial activity of the petroleum ether fraction, chloroform fraction and hydromethanol fraction from lime peel (table 1). The research results showed that the chloroform fraction provided strong antibacterial activity on all tested bacteria with the highest zone inhibition (19 mm) was observed agains *B. cereus* (Ghosh et al., 2020).

Al-Breiki et al. (2018) examined the antibacterial activity of the essential oil of lime peel which grows in three regions in Oman (Al-Batinah, Al-Sharqia, and Muscat) (table 1). At every tested concentration, Muscat region peel essential oil demonstrated the strongest antibacterial action against both pathogenic bacteria (*S. aureus* and *E. coli*), whereas Al-Sharqia peel essential oil shown the lowest activity. The differences in these essential oil chemical composition may be the reason of the diversity in antibacterial action (Al-Breiki et al., 2018).

Jeffrey et al. (2019) tested lime peel extracts and fractions against cariogenic bacteria, namely *S. mutans.* The results demonstrated that the lime peel fraction and extract had an effect on preventing the enzymatic activity of *S. mutans* from forming. The greater the zone of inhibition formed, the higher the concentration of lime peel extract or fractions (Table 1) (Jeffrey et al., 2020).

Table 2. Antibacterial activity of lime peel using agar diffusion (well) method

Microbe	Sample	Concentration	Inhibitory zone (mm)	Reference
Gram-positive bacteria				
Bacillus spp	Ethanol extract	1.0 ml of 10% v/v	23.33	(Shakya et al., 2019)
Staphylococcus aureus	Ethanol extract	1.0 ml of 10% v/v	21.66	(Shakya et al., 2019)
	Ethanol extract	20; 40; 60; 80; 100%	9; 14; 16; 18; 19	(Ekawati et al., 2019)
	Essential oil	60%, 90%	7.5; 26.5	(Edogbanya et al., 2019)
S. aureus ATCC 25923	Ethanol extract	1.0 ml of 10% v/v	21.33	(Shakya et al., 2019)
Gram-negative bacteria				
Salmonella typhi	Ethanol extract	1.0 ml of 10% v/v	20.66	(Shakya et al., 2019)
Escherichia coli	Ethanol extract	1.0 ml of 10% v/v	8.33	(Shakya et al., 2019)
E. coli ATCC 25922	Ethanol extract	1.0 ml of 10% v/v	21.33	(Shakya et al., 2019)
Psedomonas aeruginosa	Ethanol extract	1.0 ml of 10% v/v	9.33	(Shakya et al., 2019)
	Essential oil	30%, 60%, 90%	6; 14.5; 20	(Edogbanya et al., 2019)
Klebsiella pneumoniae ATCC 13883	Ethanol extract	1.0 ml of 10% v/v	18	(Shakya et al., 2019)

From research conducted by Shakya et al. (2019) it is known that the ethanol extract of lime peel has antibacterial activity against several gram-positive and gram-negative bacteria (table 2), with the strongest antibacterial activity against *Bacillus* spp (inhibition zone 23.33mm) (Shakya et al., 2019). The extract of lime peel can stop the growth of bacteria, specifically *S. aureus,* which causes skin infections Table 2). Eighty percent is the ideal dosage of lime peel extract that can stop *S. aureus* from growing in the sensitive group (Ekawati et al., 2019).

Edogbanya et al. (2019) examined the antimicrobial activity of the essential oils of three types of oranges, one of which was lime peel essential oil. The results showed that lime peel essential oil has antibacterial activity against *S. aureus* and *P. aeuginosa* (table 2) (Edogbanya et al., 2019).

Antibacterial activity of lime peel using dilution method

Table 3. Antibacterial activity of lime peel using dilution method

Microbe	Sample	MIC	MBC	Reference
Gram-positive bacteria				
Staphylococcus aureus	Methanol extract-Elachi	31.25 μg/ml	31.25 μg/ml	(Afroja et al., 2017)
	Methanol extract-Batabi	31.25 μg/ml	31.25 μg/ml	(Afroja et al., 2017)

Microbe	Sample	MIC	MBC	Reference
	Ethyl acetate extract-Elachi	750 µg/ml	750 µg/ml	(Afroja et al., 2017)
	Ethyl acetate extract-Batabi	500 µg/ml	>500 µg/ml	(Afroja et al., 2017)
Staphylococcus epidermidis	Essential oil	25%		(Nurdin et al., 2012)
Bacillus cereus	Methanol extract-Elachi	125 µg/ml	125 µg/ml	(Afroja et al., 2017)
	Methanol extract-Batabi	62.5 µg/ml	62.5 µg/ml	(Afroja et al., 2017)
	Ethyl acetate extract-Elachi	62.5 µg/ml	62.5 µg/ml	(Afroja et al., 2017)
	Ethyl acetate extract-Batabi	31.25 µg/ml	31.25 µg/ml	(Afroja et al., 2017)
Streptococcus mutans	Methanol extract	1.56%	3.12%	(Jeffrey et al., 2020)
	N-hexane fraction	0.19%	0.39%	(Jeffrey et al., 2020)
	Ethyl acetate fraction	0.78%	1.56%	(Jeffrey et al., 2020)
	Water fraction	6.25%	12.5%	(Jeffrey et al., 2020)
	Essential oil	20 µg/ml		(Lemes et al., 2018)
S. mitis	Essential oil	100 µg/ml		(Lemes et al., 2018)
S. sanguinis	Essential oil	100 µg/ml		(Lemes et al., 2018)
S. sobrinus	Essential oil	200 µg/ml		(Lemes et al., 2018)
S.salivarius	Essential oil	200 µg/ml		(Lemes et al., 2018)
Lactobacillus casei	Essential oil	31.25 µg/ml		(Lemes et al., 2018)

Table 3 is a summary of the antibacterial activity of lime peel using the dilution method. The strength of antimicrobial activity based on the MIC value can be divided into three categories: strong category with MIC value <100 µg/mL, medium with MIC value 100-625 µg/mL, and has weak activity if the MIC value is > 625 µg/mL (Dzoyem et al., 2012).

Afroja et al. (2017) tested the antibacterial activity of several orange peel extracts available in the local Bangladesh market, including Elachi and Batabi lime peels. The results showed that methanol-Elachi extract, methanol-Batabi extract had strong antibacterial activity against S. aureus, and methanol-Batabi extract, ethyl acetate-Elachi extract, ethyl acetate-Batabi extract had strong antibacterial activity against B. *cereus.* The antibacterial activity of the medium was provided by ethylacetate-Batabi extract against *S. aureus* and methanol-Elachi extract against B. cereus. Meanwhile, ethylacetate-Elachi extract provided weak antibacterial activity against S. aureus (Table 3)(Afroja et al., 2017).

Lime peel has the potential to be a valuable source of potent antibacterial agents, as it exhibits robust antibacterial activity with lower MIC values.

The lime peel essential oil was analyzed using GC-MS, which identified limonene as the primary ingredient. Lime peel essential oil was tested for antibacterial activity against cariogenic bacteria. The results showed that lime peel essential oil has strong antibacterial activity against *S. mutans* and *L. casei*, while against *S. mitis, S. sanguinis, S. sabrinus* and *S. salivarius* it has medium antibacterial activity (Table 3)(Lemes et al., 2018)

Nurdin et al. (2012) compared the antibacterial activity of lime peel essential oil with sulfur against *S. epidermidis* which causes acne. The results showed that lime peel essential oil has better antibacterial activity than sulfur with an MIC of 25%, while the sulfur MIC is 50% (Table 3) (Nurdin et al., 2012). It has long been recognized that certain essential oils, which are organic aromatic molecules derived from medicinal plants, might treat acne (Kelvin & Linda Julianti Wijayadi, 2022).

Main constituents of lime peel essential oil.

The component analysis of lime peel essential oil has been done. The method used for the content examination of the essential oil from lime peel was Gas Chromatography-Mass Spectrophotometry (GS-MS). Differences in essential oil constituents can be influenced by different growing regions, such as differences in levels or constituents of lime peel essential oil from three regions in Oman and Brazil (Table 4)(Al-Breiki et al., 2018)(Lemes et al., 2018).

Table 4. Main constituents of lime peel essential oil

Brazil (Lemes et al., 2018)	Al Batinah-Oman (Al-Breiki et al., 2018)	Al-Sharqia-Oman (Al-Breiki et al., 2018)	Muscat-Oman (Al-Breiki et al., 2018)
Limonene (77.5%)	D-Limonene (54.44%)	D-Limonene (34.464%)	D-Limonene (36.471%)
Myrcene (4.4%)	E-Citral (7.276 %)	β-Pinena (14.483%)	β-Pinena (16.749%)
Linalool (3.5%)	Z-Citral (5.81%)	β-Cymene (3.052%)	γ-Terpinene (5.220%)
Citronellal (3.2%)	γ-Terpinene (5.603%)	L-αTerpineol (1.94%)	E,E-α-Farnesene (4.781%)
Citronellol (2%)	Γ-Elemene (5.272%)	Linalool (1.866%)	α-Terpineol (3.909%)

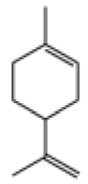

Figure 1. Main constituent of lime peel essential oil

Limonene has antibacterial capabilities by breaking the cell membranes of bacteria, ultimately causing their demise. It has long been known that essential oils can attach to the protein found on cell membranes of bacterias, increasing the permeability of those membranes. This leads to cellular content leakage and eventual cell death (Vieira et al., 2017).

Limonene is the largest component of lime peel essential oil. Limonene has antibacterial activity by damaging and increasing the permeability of bacterial cell walls (Han et al., 2021). Beside limonene, a compound in lime peel essential oil that also has antibacterial activity is linalool (Aelenei et al., 2019). Linalool destroyed the cell structure and expelled the cytoplasm by lowering the membrane potential, causing alkaline phosphatase to leak, and releasing the DNA, RNA, and proteins of bacteria (Guo et al., 2021). Potential areas for future research could include the refinement of extraction techniques, the evaluation of safety profiles, and the implementation of clinical trials to substantiate the effectiveness of products obtained from lime peel.

CONCLUSION

Numerous scientific papers included for this review demonstrated the potentially effective antibacterial properties of lime peel. Strong antibacterial activity is exhibited by lime peel essential oils, extracts, and fractions. One component of lime peel essential oils that contributes to its antibacterial properties is limonene. According to this study, infections brought on some bacteria including cariogenic bacteria and acne bacteria can be treated using lime peel.

The research on the antibacterial activity of lime peel has broader significance beyond its direct applications in medicine and agriculture. It enhances our basic comprehension of natural antimicrobial compounds and their possible function in fighting bacterial illnesses. This knowledge can be used to guide the creation of innovative treatments and goods that have wider implications for public health, environmental sustainability, and the study of natural products.

The antibacterial spectrum specificity of lime peel extracts and essential oils varies depending on the type of bacterium. Further experimentation is required on lime peel to determine its potential efficacy in treating severe illnesses.

The antibacterial spectrum specificity of lime peel extracts and essential oils varies depending on the type of bacterium. Further experimentation is required on lime peel to determine its potential efficacy in treating severe illnesses.

Future Works: Conduct extensive molecular research to elucidate the mechanisms by which the antibacterial capabilities of lime peel components, particularly limonene, function. This could involve investigating the cellular structure of bacteria, the mechanisms of enzyme function, or the process of gene expression.

Conduct comprehensive safety and toxicological examinations on lime peel extracts to ensure their suitability for human consumption. As part of this process, the adverse effects are assessed and appropriate dosage limits are established to ensure safety. To enhance the utilization of lime peel's antibacterial characteristics in agriculture, healthcare, and other domains, it is imperative to tackle these challenges and conduct further research.

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