



Literature Review: The Effect of Extra Virgin Olive Oil (*Olea europaea* L.) on *Pseudomonas aeruginosa* Bacteria

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Abstract

Background: Olive oil, especially Extra Virgin Olive Oil (EVOO), which contains polyphenols and phytochemical compounds such as flavonoids and oleuropein, has long been utilized to enhance human health and exhibits potential antibacterial activity against *Pseudomonas aeruginosa*, an opportunistic pathogenic bacterium often responsible for severe infections and resistance to various antibiotics. **Objective:** To investigate the antibacterial properties of extra virgin olive oil (*Olea europaea* L.) against *Pseudomonas aeruginosa*. **Method:** A literature review study obtained from the internet, including theses, journals, textbooks, and e-books. The databases used were Google Scholar, Elsevier, ScienceDirect, and PubMed NCBI. **Results:** Extra Virgin Olive Oil (EVOO) demonstrates antibacterial activity against *Pseudomonas aeruginosa* based on findings from 10 journals. Bioactive compounds such as polyphenols, oleuropein, and hydroxytyrosol are effective against *Pseudomonas aeruginosa* through mechanisms that include inhibiting quorum sensing, damaging the cell wall, increasing membrane permeability, and inhibiting biofilm formation and virulence factors. Olive leaf extract and combinations with nanoparticles further enhance antibacterial effectiveness against resistant strains, making EVOO a potential natural antibacterial agent. **Conclusion:** Olive oil, particularly Extra Virgin Olive Oil (EVOO), contains bioactive compounds such as oleacein, oleocanthal, polyphenols, flavonoids, oleuropein, and hydroxytyrosol, which exhibit significant antibacterial activity against *Pseudomonas aeruginosa*.

Keywords: Olive Oil; EVOO; *Pseudomonas Aeruginosa*, Bacteria

Introduction

Plant-derived products are often used to enhance human health and animal growth. Active components in oils can stimulate the immune system and increase the production of digestive enzymes. Nutrients and natural compounds, especially polyphenols and fatty acids, have been proven beneficial for body health, providing a dietary approach for the prevention and management of infectious diseases without drugs. One such example is

the Olive fruit (*Olea europaea* L.) and its derivative products, such as olive oil extracted through various methods¹.

Since the time of the Prophet, this plant has been utilized for cooking, medicinal, cosmetic, and soap-making purposes. The virtues of the Olive fruit were also conveyed by Prophet Muhammad SAW. He once recommended his followers to use the Olive fruit, saying, "Eat the Olive fruit and use it as oil" (hadith narrated by Ahmad and al-Tirmidzi). Based on the recommendation mentioned in the Al-Qur'an

and this hadith, Islamic scholars then believed that the Olive is one of the medical scientific miracles^{2,3}.

In the European Union, olive oil is classified into various types, such as Virgin Olive Oil (VOO), Extra Virgin Olive Oil (EVOO), Refined Olive Oil, Olive Pomace Oil, and Lampante Olive Oil. Specifically, EVOO, rich in glycerol or the saponifiable fraction, contributes the majority (90-99%) of monounsaturated fatty acids (MUFA) within it. MUFA is the main component, where oleic acid can reach up to 80% of the total oil. Polyunsaturated fatty acids (PUFA) usually comprise 3-22% of olive oil, while saturated fatty acids (SFA) and linoleic acid are in the range of 8-26%. Additionally, olive oil also contains small phytochemical compounds that have diverse biological benefits and contribute about 1-2% of the total composition^{4,5}.

Extra Virgin Olive Oil (EVOO) is oil extracted through a mechanical pressing process from the fruit of the Olive tree (*Olea europaea* L.). EVOO has a much higher polyphenol content compared to processed olive oil. Approximately 500 mg/L of polyphenols are found in Extra Virgin Olive Oil. The antibacterial activity in EVOO can be attributed to the content of phenolic compounds such as polyphenols, flavonoids, oleuropein, and essential oils, which have pharmacological effects on microbial activity⁶⁻⁸.

Pseudomonas aeruginosa is a gram-negative, aerobic, oxidation-positive, non-fermenting, motile bacillus bacterium found in water, soil, the rhizosphere, and animals as an opportunistic pathogen in animals and humans. This bacterium also causes infections in healthy hosts. This bacterium can tolerate various physical conditions even with minimal nutritional conditions, and forms biofilms on biotic or abiotic surfaces^{9,10}.

In the hospital environment, this microorganism is one of the most frequent and severe causes of hospital-acquired infections,

especially affecting patients with impaired immunity (especially neutropenia) and patients in intensive care units (ICU). The majority of *P. aeruginosa* strains are resistant to most currently used antibiotics. *P. aeruginosa* can be transmitted through several routes, including from patient to patient and environmental contamination. Due to its adaptable nature and high survival ability, this bacterium can survive on dry inanimate surfaces in the hospital environment from 6 hours to 6 months^{11,12}.

Currently, medical practitioners face the challenge of increasing cases of *Pseudomonas aeruginosa* infections that have resistance levels to most or even all types of β -lactam, aminoglycoside, and quinolone antibiotics. Clinical strains of *Pseudomonas aeruginosa* show resistance to various types of antibiotic agents, including β -lactams, aminoglycosides, and fluoroquinolones. Resistance in this pathogen develops due to selective pressure from mutations in chromosomal genes, resulting in the production of extended-spectrum β -lactamases (ESBL), AmpC overexpression, repression or inactivation of *oprD*, as well as overexpression of efflux pumps. Consequently, this leads to failure in overcoming infections^{13,14}.

Based on the description above, it is important to review the literature and research that have provided evidence regarding the effect of olive oil on bacteria, particularly *Pseudomonas aeruginosa*. This aims to deeply understand the antibacterial compounds contained in olive oil (*Olea europaea* L.) and their mechanism of action against these bacteria. Thus, the researchers initiated a literature review to answer the following research question: How effective is olive oil (*Olea europaea* L.) in inhibiting the growth or killing *Pseudomonas aeruginosa* bacteria? This review is expected to strengthen the understanding of the potential of olive oil as an effective antibacterial agent.

Materials and Methods

Study Design

This research is a Literature Review study that includes reviews, summaries, and analysis of the authors' thoughts regarding the discussed topic. This study was conducted by considering relevant, current, and adequate literature, covering theoretical foundations and in-depth literature reviews. Literature Review was chosen to provide a comprehensive perspective on the research topic based on credible sources using the PRISMA approach as shown in Figure 1.

Sample

The sample in this study consists of articles or literature relevant to the research topic, namely Olive Oil (*Olea europaea* L.) and *Pseudomonas aeruginosa*. Inclusion criteria include national or international articles published in the last 7 years (2017-2024), having a minimum of 20 references, and written in Indonesian or English. Exclusion criteria include articles that cannot be fully accessed, only include abstracts or introductions, and references written in languages other than Indonesian and English.

Data Collection Techniques

The data used is secondary data obtained through post-observational studies from various literature, including theses, journals, textbooks, and e-books. Literature was collected from various trusted databases, such as Google Scholar, Elsevier, Science Direct, and PubMed NCBI. Keywords used in the literature search included "Olive Oil (*Olea europaea* L.)", "Olive Oil Content", and "*Pseudomonas aeruginosa*".

Data Analysis Techniques

Data was analyzed using critical appraisal based on JBI Critical Appraisal Tools for Experimental Studies. Articles that met the inclusion criteria were analyzed to identify relevance, validity, and contribution to the

research. Ten articles that met the inclusion criteria were analyzed, with the discussion of each article presented in Table 1.

Ethical Consideration

This research conducted citation and use of literature by paying attention to research ethics and respect for the copyright of the sources used. The research pays attention to ethical principles, including ensuring all sources used are cited correctly according to academic standards, maintaining scientific integrity, and respecting the copyright and licenses of the literature used. This is done to ensure that the research is conducted responsibly and professionally.

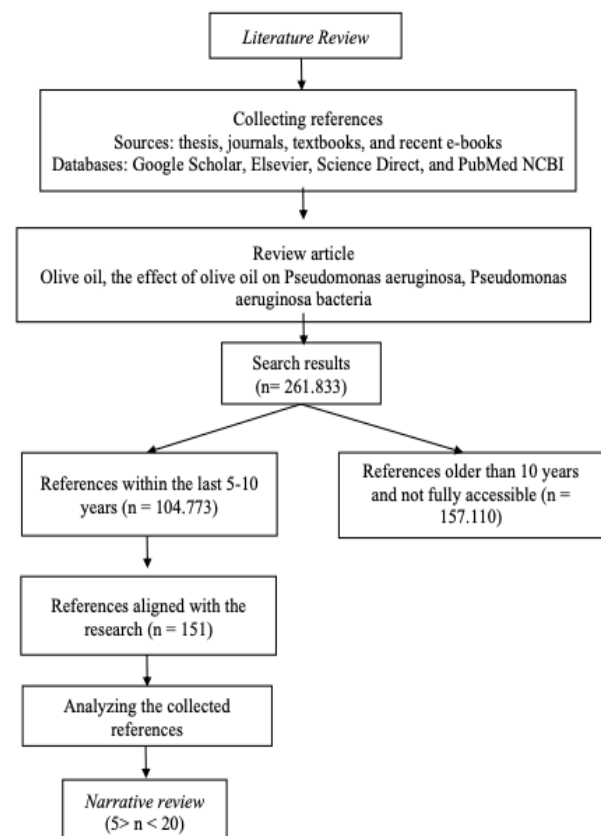


Figure 1. Article search flow using the PRISMA approach.

Result

The search results showed there were 261,833 articles, which were then filtered based on year, language, and article type until 464 articles

remained. A total of 157,110 articles were eliminated because they were published more than 10 years ago. A total of 115 articles aligned with the research objectives, and 10 articles that met the inclusion criteria were selected. These articles discussed the relationship between the content in Olive oil (*Olea Europaea* L.), the effect of olive oil (*Olea Europaea* L.) on *Pseudomonas aeruginosa* bacteria, and the mechanism of olive oil (*Olea Europaea* L.) against *Pseudomonas aeruginosa*. For research on the effectiveness of olive oil

(*Olea Europaea* L.) against *Pseudomonas aeruginosa* bacteria, the article selection process will follow a similar procedure, where articles relevant to the topic of olive oil's effectiveness against these bacteria will be filtered based on inclusion criteria including year, language, and relevance to research focusing on the effect of olive oil on *P. Aeruginosa*. This systematic selection ensures that the evidence gathered is both current and scientifically robust to support the study's conclusions.

Table 1. Review Search Results According to Research Problem (Effectiveness of Olive Oil (*Olea Europaea* L.) against *Pseudomonas Aeruginosa* bacteria)

No.	Author, Title, Year of Research	Research Findings	Research Conclusion
1.	Jon E. Paczkowski, Sampri Mukherjee, Amelia R. McCready, Jian-Ping Cong, Christopher J. Aquino, Hahn Kim, Brad R. Henke, Chari D. Smith, and Bonnie L. Bassler; Flavonoids Suppress <i>Pseudomonas aeruginosa</i> Virulence through Allosteric Inhibition of Quorum-sensing Receptors (2017)	Three flavonoids (phloretin, chrysin, naringenin) were identified as effective QS inhibitors against LasR and RhlR, inhibiting the activity of both targets without affecting cell growth. Structure-activity of flavonoids showed that two hydroxyl groups on ring A at positions 5 and 7 are important for inhibitory activity. Flavonoids work non-competitively, inhibiting LasR binding to DNA without competing with AutoInducer (AI) at the LasR binding site. Analysis showed flavonoids interact allosterically on the ligand-binding domain (LBD) of LasR, without disrupting LasR dimerization. In vivo effects on <i>P. aeruginosa</i> include decreased <i>rhIA</i> gene expression, reduced pyocyanin production, and inhibition of swarming, without affecting bacterial growth, showing high specificity.	Flavonoids have great potential as alternative anti-virulence agents, which do not inhibit bacterial growth, thus reducing antibiotic resistance selection, so flavonoids can be developed as new anti-infection therapies to inhibit bacterial virulence, not kill bacteria.
2.	Haifaa Bawie Najee, Dunya Alkurjia, Othman Almahdawy, Crina Kamerzan, Luminita Marutescu Irina Gheorghe, Marcela Popa, Mariana Carmen Chifiriuc, Veronica Lazăr; Antimicrobial Activity of <i>Olea europaea</i> Fatty Oil against Multi-Drug Resistant	Antimicrobial activity testing of olive oil using the Broth Microdilution Assay method showed varying MIC, with <i>S. aureus</i> being the most susceptible (5.23 mg/mL) and <i>P. aeruginosa</i> the most resistant (41.8 mg/mL). Antibiofilm testing via Microtiter Plate Assay showed the most effective MBEC on <i>S. aureus</i> (1.31 mg/mL), while <i>P.</i>	Olive oil (<i>Olea europaea</i>) shows significant antimicrobial and antibiofilm activity against MDR bacteria and fungi, especially against <i>P. aeruginosa</i> .

No.	Author, Title, Year of Research	Research Findings	Research Conclusion
	and Biofilm Forming Microorganisms; (2018)	aeruginosa and <i>C. albicans</i> had higher resistance (>41.8 mg/mL). Antibiofilm activity was associated with oleuropein content (73.41%). Analysis of antimicrobial mechanism using Flow Cytometry (FCM) showed cell membrane damage and efflux pump inhibition, marked by increased fluorescence due to EB dye accumulation within cells.	
3.	Nazanin Pasandideh and Masoumeh Anvari; Study on antimicrobial effects of <i>Olea europaea</i> (Olive) and olive leaf extracts on pathogenic bacteria using Taguchi methodology; (2018)	This study assessed the antimicrobial activity of olive leaf and fruit extracts against <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , and <i>Pseudomonas aeruginosa</i> . From the Taguchi experimental design, the results were: Longer incubation time (6 hours) had a significant effect on increasing antimicrobial activity ($p = 0.001$). Olive leaf extract was more effective than fruit and olive oil. <i>Staphylococcus aureus</i> was most susceptible to the extract, while <i>Escherichia coli</i> was the most resistant. Black leaf and mari leaf showed the best antimicrobial activity.	This study shows that <i>Olea europaea</i> products have the potential to be developed into herbal antimicrobial drugs to fight pathogenic bacteria.
4.	Filomena Nazzaro, Florinda Fratianni, Rosaria Cozzolino, Antonella Martignetti, Livia Malorni, Vincenzo De Feo, Adriano G. Cruz and Antonio d'Acierno; Antibacterial Activity of Three Extra Virgin Olive Oils of the Campania Region, Southern Italy, Related to Their Polyphenol Content and Composition; (2019)	The antibacterial activity of three polyphenol extracts (PF) from EVOO varieties Ogliarola, Ravece, and Ruvea Antica was tested against <i>P. aeruginosa</i> using the inhibition zone test. Results showed that Ogliarola produced inhibition zones of 6.33 mm and 11.33 mm, Ravece 8.67 mm and 16.33 mm, and Ruvea Antica 4.33 mm and 6.67 mm. The highest antibacterial activity was found in the Ravece variety, showing the ability of polyphenols to penetrate Gram-negative bacterial membranes. MIC testing showed very strong antibacterial effectiveness (1.00 µg/mL) in Ogliarola and Ravece. The main polyphenol composition identified included Oleuropein, Quercetin, Luteolin, Catechin, and Naringenin, with Formononetin and Quercetin having the highest correlation to antibacterial activity.	Ogliarola and Ravece varieties have the highest antibacterial activity against <i>Bacillus cereus</i> and <i>Pseudomonas aeruginosa</i> , associated with polyphenol content, especially quercetin and formononetin. Meanwhile, the Ruvea Antica variety showed lower antibacterial activity due to lower polyphenol content. All three polyphenol extracts effectively inhibited the growth of <i>Pseudomonas aeruginosa</i> .

No.	Author, Title, Year of Research	Research Findings	Research Conclusion
5.	Hiba Qasim Hameed, Anaam Abdulqader Hasan, Rana Mujahid Abdullah; Effect of Olea europea L Extraction and TiO ₂ Nanoparticles against Pseudomonas aeruginosa; (2019)	This study evaluated the antibacterial efficacy of titanium dioxide nanoparticles (TiO ₂) and olive leaf extract against three isolates of Pseudomonas aeruginosa. TiO ₂ was effective against isolate 1, but had minimal impact on isolates 2 and 3. Olive leaf extract showed broad-spectrum antibacterial activity against all three isolates, with a synergistic effect observed when combined with TiO ₂ . Active compounds in olive leaf extract, such as flavonoids, phenols, alkaloids, tannins, fatty acids, and steroids, increased cell wall damage and inhibited bacterial cell metabolism. X-ray diffraction analysis confirmed the small size of TiO ₂ nanoparticles, contributing to their antibacterial potential.	Olive leaf extract shows significant antibacterial activity, enhanced by TiO ₂ nanoparticles which increase the penetration of active compounds into bacterial cells, accelerating their antibacterial action.
6.	Nazly R. El-sayed, Reham Samir, Lina Jamil M. Abdel-Hafez, and Mohammed A. Ramadan; Olive Leaf Extract Modulates Quorum Sensing Genes and Biofilm Formation in Multi-Drug Resistant Pseudomonas aeruginosa; (2020)	Susceptibility testing showed that 49% of isolates were multidrug-resistant, and over 90% formed biofilms, with 26% of them being strong biofilm producers. Green tea and olive leaf extracts inhibited biofilms up to 84.8% and 82.2%, respectively, at sub-inhibitory concentrations. Expression of lasI, lasR, rhlI, and rhlR genes decreased significantly ($p < 0.05$) by approximately 97–99%. Olive leaf extract contains bioactive compounds such as oleuropein and hydroxytyrosol that damage bacterial cell membranes and inhibit biofilm formation. This extract also reduced pyocyanin production by up to 40.8% (C21) and 47.6% (E81), which are harmful to host cells.	This study shows that green tea and olive leaf extracts are effective against planktonic cells and biofilms of MDR Pseudomonas aeruginosa, inhibiting biofilm formation, twitching motility, and pyocyanin production. Both extracts are also cheap, abundant, and renewable sources of biophenols.
7.	Dragana Borjan, Maja Leitgeb, Željko Knez and Maša Knez Hrnčič; Microbiological and Antioxidant Activity of Phenolic Compounds in Olive Leaf Extract; (2020)	Olive leaf extract contains various bioactive compounds that play important roles in its biological activity: Oleuropein obtained has strong antimicrobial and antioxidant activity. Hydroxytyrosol, a derivative of oleuropein with a catechol-like structure soluble in water and fat, plays an important role in cardiovascular protection, neuroprotection, antitumor, and antioxidant activity. Then β -glucosidase enzyme in olive leaves	Olive leaf extract, rich in phenolic compounds such as oleuropein and hydroxytyrosol, has great potential in inhibiting pathogenic microorganisms and scavenging free radicals. This antimicrobial and antioxidant activity makes it a promising candidate for treating microbial infections and antioxidant protection.

No.	Author, Title, Year of Research	Research Findings	Research Conclusion
		plays a role in converting oleuropein into its aglycone form, increasing antimicrobial and antioxidant effectiveness. Research shows olive leaf extract effectively inhibits the growth of various pathogenic microorganisms, including Gram-positive, Gram-negative bacteria, and fungi.	
8.	Marisa Di Pietro, Simone Filardo, Roberto Mattioli, Antonio Francioso, Giammarco Raponi, Luciana Mosca and Rosa Sessa; Extra Virgin Olive Oil-Based Green Formulations with Promising Antimicrobial Activity Against Drug-Resistant Isolates; (2022)	Antimicrobial activity of various green-based extra virgin olive oil formulations in deep eutectic solvents (NaDESs) that emerge as strong and biocompatible solvents. Specifically, the antimicrobial activity of EVOO extract, as well as purified oleocanthal and oleacein in two NaDES (choline/glycerol and choline/propylene glycol), against several drug-resistant clinical isolates and standard microbial strains has been evaluated. The main results are the inhibitory activity of EVOO extract in choline/glycerol and oleacein in choline/propylene glycol against drug-resistant Gram-positive and Gram-negative strains. Oleacein in choline/propylene glycol was the most effective against various clinical strains of <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , and <i>Klebsiella pneumoniae</i> . Additionally, all tested formulations were effective against <i>Candida</i> spp.	EVOO extract in choline/glycerol and oleacein in choline/propylene glycol show great potential against drug-resistant bacterial and fungal strains. Antimicrobial activity is influenced by the combination of polyphenols (oleacein, oleocanthal) and the solvent properties of NaDES that enhance the bioavailability of bioactive compounds, thus increasing antimicrobial effectiveness compared to methanol solvent formulations.
9.	Hafez Al-Momani, Dua'a Al Balawi, Saja Hamed, Borhan Aldeen Albiss, Muna Almasri, Hadeel AlGhawrie, Lujain Ibrahim, Hadeel Al Balawi, Sameer Al Haj Mahmoud, Jeffrey Pearson & Christopher Ward; The impact of biosynthesized ZnO nanoparticles from <i>Olea europaea</i> (Common Olive) on <i>Pseudomonas aeruginosa</i> growth and biofilm formation; (2023)	Zinc Oxide nanoparticles (ZnO NPs) synthesized with a crystalline size of about 42 nm, as determined by X-ray diffraction, showed significant antimicrobial effects against <i>Pseudomonas aeruginosa</i> (PA) strains. Scanning electron microscopy revealed ZnO NPs with an average size of 50 nm. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of ZnO NPs were 3 mg/ml and 6 mg/ml, respectively. ZnO NPs effectively inhibited planktonic growth as well as biofilm formation in PA strains, with significant reduction in biofilm biomass and metabolic activity at concentrations of 400–1000 µg/ml.	This study concludes that Zinc Oxide nanoparticles (ZnO NPs) show significant antibacterial properties against <i>Pseudomonas aeruginosa</i> (PA) strains, including those resistant to conventional antibiotics.

No.	Author, Title, Year of Research	Research Findings	Research Conclusion
10.	Marisa Di Pietro, Simone Filardo, Roberto Mattioli, Giuseppina Bozzuto, Giammarco Raponi, Luciana Mosca, and Rosa Sessa; Anti-Biofilm Activity of Oleacein and Oleocanthal from Extra-Virgin Olive Oil toward <i>Pseudomonas aeruginosa</i> ; (2024)	Additionally, ZnO NPs affected the expression of genes regulated by quorum sensing, reducing levels of <i>lasI</i>, <i>lasR</i>, <i>rhlI</i>, <i>rhlR</i>, <i>pqsR</i>, and <i>pqsA</i>, especially at higher concentrations (900 µg/ml). This shows that ZnO NPs have strong antibacterial and biofilm-disrupting properties, as well as effects on quorum sensing in PA. The main results of our study are the anti-virulence activity of a mixture of oleacein and oleocanthal against multidrug-resistant and intermediate-resistant <i>P. aeruginosa</i> strains isolated from patients with ventilator-associated pneumonia or surgical site infections. Specifically, a mixture of oleacein (2.5 mM) and oleocanthal (2.5 mM) significantly inhibited biofilm formation, alginate and pyocyanin production, as well as motility in both <i>P. aeruginosa</i> strains ($p < 0.05$). Further scanning electron microscopy analysis showed its ability to inhibit bacterial cell adhesion as well as extracellular matrix production.	Combination of oleacein and oleocanthal effectively reduces biofilm, alginate production, pyocyanin, and bacterial motility without targeting direct growth. This can reduce the risk of further bacterial resistance.

Discussion

Olive Oil Content as Antibacterial

Extra virgin olive oil (EVOO) has a polyphenol content that contributes to its biological properties, including antibacterial activity; some compounds contained in polyphenols are oleuropein, flavonoids, hydroxytyrosol, and other compounds. Jon E. Paczkowski, et al (2017) found from the identification of QS inhibitors that there are three flavonoids (phloretin, chrysin, naringenin) that act as effective QS inhibitors against LasR and RhIR as dual-targets without affecting cell growth in *P. aeruginosa* ¹⁶.

H. Qasim Hameed, et al (2019) showed that active compounds flavonoids and phenols have the ability to damage bacterial cell walls, Alkaloids and tannins work by inhibiting

important enzymes in bacterial cell metabolism, fatty acids and steroids cause increased permeability of bacterial cell membranes, thus disrupting cell function ¹⁶. These combined mechanisms demonstrate that secondary metabolites play a crucial role as natural antibacterial agents with broad-spectrum potential

Haifa Bawie, et al (2018) showed that the antibiofilm activity of olive oil is associated with the high oleuropein content (73.41%) in olive oil. Nazanin P., et al (2018) found that all olive products such as olive oil, olive leaf extract have high potential as natural antimicrobial agents because of the oleuropein content which is bacteriostatic against various types of bacteria both gram positive and gram negative. Dragana Borjan, et al (2020) showed that the oleuropein content obtained has strong

antimicrobial and antioxidant activity, and hydroxytyrosol content which is a derivative of oleuropein with a catechol-like structure soluble in water and fat that plays an important role in cardiovascular protection, neuroprotection, antitumor and antioxidant activity¹⁶.

Marisa Di Pietro, et al (2022) showed that the combination of polyphenols (oleacein, oleocanthal) and NaDES solvent properties can increase the bioavailability of bioactive compounds. Hafez Al-momani, et al (2023) concluded that Zinc Oxide nanoparticles (ZnO NPs), biosynthetically synthesized from *Olea europaea* and characterized show significant antibacterial properties including those resistant to conventional antibiotics.¹⁶ Marisa Di Pietro, et al (2024) showed that specifically, a mixture of oleacein (2.5 mM) and oleocanthal (2.5 mM) significantly inhibited biofilm formation, alginate and pyocyanin production, as well as motility in both *P. aeruginosa* strains ($p < 0.05$)¹⁶.

Antibacterial Activity of Olive Oil

Olive oil shows significant antibacterial activity against *Pseudomonas aeruginosa*, although the level of effectiveness can vary based on the extraction method and concentration used. Haifaa Bawie, et al (2018) showed that olive oil has a MIC (Minimal Inhibitory Concentration) varying from 5.23 mg/ml to >41.8 mg/ml against *Pseudomonas aeruginosa* isolates. The performance of this olive oil could be caused by its ability to damage microbial cell walls, as detected by staining with Propidium Iodide (PI) and Ethidium Bromide (EB), showing increased permeability of microbial cell membranes at sub-MIC concentrations¹⁶.

Journals by Filomena N, et al (2019) and Marisa Di Pietro, et al (2022) also confirmed that olive oil extract, especially those containing polyphenols and bioactive compounds such as oleacein and oleocanthal,

are effective against *Pseudomonas aeruginosa*. Filomena N, et al (2019) reported that polyphenol extracts from extra virgin olive oil (EVOO) can inhibit the growth of *Pseudomonas aeruginosa*, while Marisa Di Pietro, et al (2022) showed that EVOO extract in NaDES (Natural Deep Eutectic Solvents) has antibacterial activity against various strains of *Pseudomonas aeruginosa*, including those resistant to drugs^{17,18}.

Inhibition of Biofilm Formation

Biofilm formation is an important factor in the virulence of *Pseudomonas aeruginosa* and resistance to treatment. Nazly R, et al (2020) and Marisa Di Pietro, et al (2024) showed that olive oil and polyphenol extracts from olive oil are effective in inhibiting *Pseudomonas aeruginosa* biofilm formation. Nazly R, et al (2020) reported that olive oil extract can inhibit biofilm formation on clinical isolates of *Pseudomonas aeruginosa* up to 82.2% at sub-MIC concentrations. Marisa Di Pietro, et al (2024) highlighted that a mixture of oleacein and oleocanthal from EVOO inhibits biofilm formation and reduces the production of virulence factors such as alginate and pyocyanin up to 90% and 63%, respectively^{19,20}.

Antimicrobial Activity of Olive Leaf Extract

Several studies show that olive leaf extract also has significant antibacterial activity against *Pseudomonas aeruginosa*. Nazanin P, et al (2018) and Dragana Borjan, et al (2020) noted that olive leaf extract has antibacterial potential against *Pseudomonas aeruginosa*. Nazanin P, et al (2018) indicated that olive leaf extract shows greater antibacterial activity compared to olive oil. Dragana Borjan, et al (2020) added that phenolic compounds from olive leaf extract, such as oleuropein and hydroxytyrosol, contribute to antibacterial activity against *Pseudomonas aeruginosa*^{21,22}.

Combination Effect with Nanoparticles

Hiba Qasim H, et al (2019) and Hafez Al-Momani, et al (2023) showed that the combination of nanoparticles with olive leaf extract can enhance antibacterial and biofilm inhibition effects. Hiba Qasim H, et al (2019) reported that the combination of titanium dioxide nanoparticles (TiO₂) and olive leaf extract showed better antibacterial activity against *Pseudomonas aeruginosa* isolates compared to using each agent separately. Similarly, Hafez Al-Momani, et al (2023) showed that zinc oxide nanoparticles (ZnO) can inhibit the growth and biofilm formation of *Pseudomonas aeruginosa*, including clinical strains, and this effect can be enhanced by combination with extracts from plants such as olive leaves^{23,24}.

Mechanism of Action

The mechanism of action of olive oil and its extracts against *Pseudomonas aeruginosa* includes several aspects. Based on Jon E, et al (2017), olive oil damages microbial cell membranes, leading to increased permeability, because flavonoid compounds inhibit QS of *P. aeruginosa* by interacting with LasR and RhlR receptors as dual-targets without affecting cell growth, flavonoids. In Vivo effects on *P. aeruginosa* significantly: Suppresses *rhlA* gene expression (using *PrhlA*-mNeonGreen reporter). Reduces pyocyanin production, an important virulence factor. Inhibits the swarming ability of bacteria on agar media¹⁶.

Haifaa Bawie, et al (2018) showed the mechanism of action of olive oil on microbial cell membrane damage and efflux pump activity, namely the presence of significant increased fluorescence in microbes given olive oil indicates Cell membrane damage (PI/EB dyes can penetrate permeable cells) and Inhibition of efflux pump (Decreased ability of microbes to expel EB, causing accumulation inside the cell)^{16,25}.

Nazly R, et al (2020) also showed that olive leaf extract can inhibit the expression of

quorum sensing (QS) related genes, suppress pyocyanin (toxic pigment that can damage host cells) in *Pseudomonas aeruginosa*, which contributes to the reduction of virulence factors and biofilm formation^{19,26}.

Conclusion

Based on the literature review results and discussion above, it can be concluded that olive oil contains bioactive compounds such as oleacein, oleocanthal, and polyphenols (oleuropein, flavonoids, hydroxytyrosol, phenols) that have significant antibacterial activity against *Pseudomonas aeruginosa*, including inhibition of planktonic growth and biofilm formation. The antibacterial mechanism involves damage to bacterial cell walls and interference with the quorum sensing system through reduction of virulence factors and biofilm formation. As a follow-up, it is suggested to test the effectiveness of olive oil against antibiotic-resistant *Pseudomonas aeruginosa* isolates and to develop more stable and effective olive oil formulations for health products, such as ointments, creams, or antiseptic solutions.

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