Review Article

Antibacterial Activity of Plant-based Essential Oils against Uropathogenic Bacteria: A Systematic Review

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ABSTRACT

Since urinary tract infections are still prevalent in today's world, the authors sought to examine and summarize current and existing data of essential oils' antibacterial activity and efficacy against a range of uropathogenic bacteria in order to educate the public about their presence and give additional information for future studies. Essential oil components have been studied in a variety of aromatic and medicinal plants. These are concentrated extracts of flowers and plants. To investigate if essential oils have a synergistic impact against human infections, they can be extracted and evaluated separately or in combination. This systematic review looks at previously recognized uropathogenic bacteria associated with infections in the urinary tract and other uropathogenic disorders that have been studied. This article discusses two types of bacteria: gram positive and gram-negative bacteria. Following the eligibility criteria, the authors conducted a systematic evaluation of literature concerning essential oils and their antibacterial efficacy against uropathogenic bacteria. Only 1,525 of the 1,574 articles found passed the screening process, and only 26 satisfied the inclusion criterion. When it comes to essential oil treatment, *S. aureus* is the most susceptible of all the gram-positive bacteria. In the meanwhile, the gram-negative bacteria *E. coli* was shown to be the most susceptible of all gram-negative bacteria. Essential oils appear to be useful medicinal plants for preventing bacterial development, according to current findings. Considering resistance to various antibiotics has become a severe concern in the recent years, the author suggests that new medical treatment for these diseases be created or improved.

Keywords: Essential oils, Uropathogenic bacteria, Synergistic, Susceptible, Urinary tract infection.

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INTRODUCTION

Essential oils are currently being recognized for enhancing the quality of life and alleviating a variety of illnesses. Multiple antibacterial properties of plants that contribute in suppressing uropathogenic invasion is one of the main strategies to entirely decrease and possibly eliminate bacterial progression. Some studies have shown that plant-based essential oils have a synergistic effect, and some have antimicrobial effects on their own. These oils have the potential to break through some bacterial membranes and defenses such as biofilms. Antibacterial components can be found in various parts, particularly the roots, flowers, stems etc. Some of the phytochemical constituents that exhibit antibacterial activity include terpenoids, tannins, alkaloids, flavonoids, and more.[1]

Urinary Tract Infection (UTI) is the commonly diagnosed renal disease infection that occurs when bacteria enter the urethra and infect the urinary system. Both gram-positive and gram-negative uropathogens are known to cause the disease. *E. coli* is the most common organism that causes the mentioned disease. Urinary Tract Infection pathogenesis is a complex

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process determined and guided by host biological and behavioral factors and properties of the infecting pathogens (virulence factors). Urine is ordinarily sterile, and any bacterial growth occurs in the urethra, where the infection begins. Researchers observed that the infection begins in the lower urinary tract, as it infects the urethra and bladder, and then progresses to the upper urinary tract, infecting the ureter and kidney. There are a lot of UTIs, four of which are: cystitis, acute renal failure, and urethritis. Urine blockage, urinary retention caused by neurological disease, renal failure, renal transplantation, pregnancy, and the presence of foreign bodies such as calculi, and prolonged use of urinary catheters are all indications of complicated UTIs. Treatment for UTIs depends on whether it is bacterial, viral or fungal. Bacterial UTIs are usually treated with antibiotics, as viral UTIs with antiviral, and fungal UTIs with antifungals. UTIs may usually be treated effectively without causing kidney damage, but if left untreated, UTIs caused by an enlarged prostate gland in males, or a kidney stone can cause kidney damage.

The core concern of the study is to discuss direct evidence of antibacterial action of essential oils against uropathogenic bacteria. This would examine and assess published journals among their synergistic effects and uroprotective properties to suppress emergence of bacterial growth in the genitourinary tract.

Metabolically active uropathogens have been turned into one of the critical health care importance in combining multiple antibacterial properties of plants to combat uropathogenic invasion. Through a systematic review process of available published articles online, this study would be necessary for contributing to the determination of plant-based essential oils that fully inhibit virulence factors that affect the host defense system while considering its individual efficacy and reducing toxicity at the same time.

MATERIALS AND METHODS

Literature Search

Most of the articles that the authors have gathered are international articles that are written in English. The literature search was comprehensively done using various general databases such as PubMed, Google Scholar, EBSCO, and ScienceDirect. Moreover, some more of the specific common article databases used to gather the journals were MDPI, Research Gate, and SagePub. Articles searched systematically were from 2015 up to date to provide more updated information on single and blended essential oils against uropathogenic bacteria. These databases are all included in the inclusion criteria for this review.

Keywords

Combinations of search terms include the terms "essential oils", "plant-based essential oils", "combined extracts", "antibacterial activity", "uropathogenic bacteria", and "urinary tract infection" for the studies focusing essential oils against uropathogens.

Eligibility Criteria

The researchers manually screened the titles and abstracts of articles and journals to assess the papers concerning the topic of interest.

The inclusion criteria for this mini review were gathered from (1) reputable sources published from 2015 - present. Additional inclusion criteria are (2) Experimental studies and (3) publications that include investigations on antibacterial activity of plant-based essential oils, (4) its uses against uropathogenic bacteria and (5) criteria for microorganisms that are usually found in the genitourinary tract, as well as the (6) disorders associated with each uropathogen.

The exclusion criteria for this mini review were consist of (1) sources published prior from 2015, (2) case studies, (3) review paper (4) research articles with no full text, (5) articles not written in English text, (6) non-uropathogenic bacteria, (7) non-uropathogen related diseases/infection, (8) topics with non-antimicrobial activity and (9) studies that are not related to mini review. Screening of articles was done by 8 authors (AA, CD, ME, FG, SN, RN, KS, AY). Final screening of articles were done by 4 authors, (AA, DB, SN, RN).

Selection Strategy

The researchers thoroughly retrieved, screened, and reviewed all journal articles in accordance with the inclusion and exclusion criteria. The contents were examined in terms of the abstract of the study, the validity of the methods used, and the applicability of the generated results to the researchers' field of interest.

The authors identified 1574 articles from different research databases. With the use of pre-specified exclusion criteria, 1505 studies were excluded and 49 were identified as duplicates.

20 articles were assessed based on the inclusion criteria, which were experimental studies that investigate on antibacterial activity of plant-based essential oils, pathogens of the genitourinary tract, effects and use on uropathogenic bacteria, and disorders associated

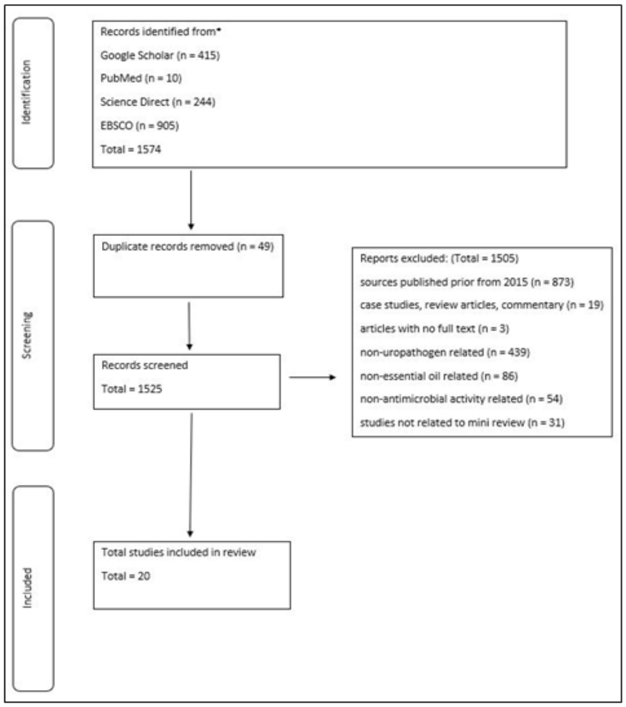

Figure 1: Illustrates the schematic diagram of the study selection process.

with each uropathogen. A schematic diagram of the study selection process is shown in Figure 1.

Data extraction

For the aim of standardization, data such as year of study, study type used, type of organism isolated, diseases involved, and methods of identification used were extracted from the included publications. Data extraction was done by 8 authors (AA, CD, ME, FG, SN, RN, KS, AY) and was approved by (AA, ME, SN, RN), and checked by (DB) for accuracy and finalization.

The articles in the study covered two kinds of essential oils: single plant-based essential oils and blended essential oils. A total of 20 articles were selected for screening. According to the eligibility criteria, 17 of the accepted articles are single plant-based essential oils and 3 are blended plant-based essential oils.

A list of accepted articles for single and plant-based essential oils and their activity against uropathogens are shown in Table 1 and 2, respectively.

RESULTS

Search Results

There were a total 1574 articles identified for this study. There were various databases used to source out the articles such as Google Scholar, PubMed, Science Direct, and EBSCO. Out of those 1574 articles, a total of 905 of them were identified from EBSCO. 415 articles were gathered from Google Scholar. From Science Direct, on the other hand, there were 244 articles picked out. Lastly, from PubMed, there were only 10 articles identified from that database.

Out of the 1574 articles, 49 duplicate entries and 1505 articles were removed based on the given criteria that would be considered eligible in this study. 1505 sources that were excluded in this review comprised 873 articles that are published prior from 2015, 19 are case studies, review articles, and commentaries, 3 of which have no full text, 439 have focused on non-uropathogenic bacteria, 86 of which are non-essential oil related, 54 of those are topics with non-antimicrobial activity, and 31 are considered unrelated to this scope of the topic. 20 articles, on the other hand, have been included, have met the criteria and will be eligible for the review.

Table 1: List of accepted articles involving single and blended plant-based essential oils.

Essential Oils	# of articles accepted	Reference
Single Plant-Based Essential Oils	17	Abreu *et al*. 2015 Ahmadian *et al*. 2020 Al Zuhairi *et al*., 2020 Bashir *et al*. 2020 Bozkurt *et al*. 2017 Das *et al*. 2018 Ginting *et al*., 2021 Firmino *et al*. 2018 Lagha *et al*. 2019 Missanjo *et al*. 2015 Moustafa *et al*. 2019 Qaralleh *et al*. 2018 Scazzocchio *et al*. 2017 Shanaida *et al*. 2021 Tibyangye *et al*. 2015 Wang *et al*., 2019 Zakaria Nabti *et al*., 2020
Blended Plant-Based Essential Oils	3	Brochot *et al*. 2017 Chitemerere *et al*. 2016 Kachkoul *et al*. 2021

Characteristics of included articles

The articles included in this study represented two of the many kinds of essential oils: Single plant-based essential oils and blended essential oils. There are a total of twenty (20) articles included from the screening of articles. Seventeen (17) of the articles are single plant-based essential oils and three (3) from the accepted articles are blended plant-based essential oils as shown in Table 1. The uses and activity of the essential oils against uropathogens are indicated in Table 2.

Table 2: List of accepted articles involving plant-based essential oils and their activity against uropathogens.

Essential Oils	Bacteria	Result Activity	Reference
Piper aduncum L.	*E. coli,* *S. aureus,* *C. albicans*	*S. aureus* and *C. albicans* are the most sensitive to Piperaceae essential oil	Abreu *et al*., 2015
Eryngium caucasicum *Froriepia subpinnata*	*E. coli*	*Froriepia subpinnata* essential oil had more antimicrobial potency	Ahmadian *et al*., 2020
Origanum glandulosum	*S. aureus,* *K. pneumoniae, P. vulgaris*	Essential oil from the Bordj location showed highest antibacterial activity	Al Zuhairi *et al*., 2020
Cymbopogon citratus	*S. aureus, P. aeruginosa* *K. pneumoniae and E. coli*	Alternative remedy to avoid damage from resistance strains	Bashir *et al*., 2020
Citrus spp.	*E. coli, S. aureus,*	*C. sinensis* L. Osbeck exhibited the highest antimicrobial activity	Bozkurt *et al*., 2017
Cinnamomum zeylanicum, Daucus carota, *Eucalyptus globulus and Rosmarinus officinalis* *Citrus limon, Lavandula angustifolia*	*E. coli, K. pneumoniae,* *P. mirabilis, P. aeruginosa*	Blended of essential oils has antibacterial activity to a wide range of bacteria including uropathogens	Brochot *et al*., 2017
Callistemon citrinus Vernonia adoensis	*S. aureus, P. aeruginosa*	*C. citrinus* alkaloid extract showed more potent growth inhibitory activity than that from *V. adoensis* with some bactericidal effects	Chitemerere *et al*., 2016
Hemidesmus indicus	*E. coli, S. aureus and* *E. faecalis*	*H. indicus* root extract is seen to be most effective against *S. aureus*	Das *et al., 2018*
Cinnamomum zeylanicum, Cinnamomum cassia	*E. coli, P. aeruginosa*	Exhibited antibacterial activities	Firmino *et al*., 2018
Syzgium aromaticum, *Cinnamomum burmannii*	*E. coli, K. pneumoniae*	Both are effective antibacterial agents against *E. coli* and *K. pneumoniae* isolates	Ginting *et al*., 2021
Eucalyptus camaldulensis, Mentha pulegium, *Rosmarinus officinalis*	*P. mirabilis, K. pneumoniae, S. aureus*	Highest IZ values were recorded for Cinnamomum zeylanicum against UTI bacterial isolates	Kachkoul *et al*., 2021
Origanum majorana, Thymus zygis, Rosmarinus officinalis, Juniperus communis, Zingiber officinale	*E. coli*	Optimal mixtures showed a synergistic effect of essential oils against bacterial strains	Lagha *et al*., 2019
Corymbia citriodora	*E. coli, S. aureus*	*C. citriodora* leaves has antimicrobial activity against both E. coli and S. aureus	Missanjo *et al.* 2015

continued...

Table 2: List of accepted articles involving plant-based essential oils and their activity against uropathogens.

Essential Oils	Bacteria	Result Activity	Reference
Cymbopogon citratus, Origanum vulgare Azadirachta indica, Zingiber officinale Syzygium aromaticum, Rosmarinus officinalis Pimpinella, anisum, Thymus vulgaris, Lavandula spica, and Cinnamomum verum	*E. coli*	*Origanum vulgare* and *Syzygium aromaticum* are active against multidrug-resistant UPEC	Moustafa *et al.*, 2019
Origanum ramonense	*S. aureus, S. epidermidis, K. pneumoniae and E. aerogenes, E. coli, P. mirabilis P. aeruginosa*	*O. ramonense* bacteriostatic and bactericidal effects indicates potent antibacterial activity	Qaralleh *et al., 2018*
Coriandrum sativum L., Apiaceae	*E. coli*	Coriander is a potential antimicrobial agent against *E. coli*	Scazzocchio *et al.*, 2017
Salvia sclarea L., *Monarda didyma, Thymus pulegioides, Thymus vulgaris, Thymus serpyllum* L.	*E. coli, S. aureus*	*Lamiaceae* species have considerable antimicrobial activity, especially against *S. aureus*	Shanaida *et al.*, 2021
Ocimum suave	*E. coli, K. pneumoniae, S. aureus, P. aeruginosa*	*O. suave* exhibited antibacterial activity to almost all uropathogens tested	Tibyangye *et al.*, 2015
Melaleuca bractreata	*E. coli, S. marcescens, Pseudomonas* spp., *S. aureus, P. aeruginosa*	*S. aureus* and *S. marcescens* had the highest sensitivity to *Melaleuca bractreata* *P. aeruginosa* had the highest resistance	Wang *et al.*, 2019
O. glandulosum Desf.	*E. coli*	The essential oils were active against all the strains	Zakaria Nabti *et al.*, 2020

DISCUSSION

Essential oils are known to be complex volatile compounds which are produced naturally in various plants. These oils have a promising activity in biomedicine since they can effectively destroy a variety of bacterial, viral, and fungal microorganisms. Given the possibility for bacterial diseases if uropathogenic infections are not treated, identifying these essential oils and their active chemical components might be a life-saving strategy for ensuring adequate medical treatment.

The authors' aim was to examine the antibacterial potential of essential oils against uropathogenic infections after analyzing several studies on essential oil extraction. It is crucial to observe which essential oils are most active and efficient against specific gram-positive and gram-negative uropathogens. Moreover, this review highlights the results of plant-based essential oils tested with broth microdilution assay and disc diffusion.

Effectiveness of Essential Oils on Gram-positive Bacteria

Gram-positive bacteria have a thick and multilayered peptidoglycan layer and retain crystal violet during gram staining. Beyond their peptidoglycan membrane, these bacteria lack an exterior cell wall, making them more absorbent. Antibiotics including penicillin, erythromycin, and cloxacillin are used to treat 90% of gram-positive bacteria. Antibiotic resistance is, however, becoming a major issue with these gram-positive infections.[2] Determining the effectiveness of these EO requires knowing the susceptibility and resistance of the uropathogens. Susceptible means that the bacteria cannot grow if the antibacterial agent is present, meaning the agent is capable of killing the bacteria. Meanwhile, resistance refers to the ability of the bacteria to proliferate despite the presence of the antibiotic. This is an indication of an agent that is not working.

In most of the studies, *Staphylococcus aureus* (SA) was shown to be the most susceptible gram positive uropathogen. Investigation of Alzuhairi *et al*. 's (2020) study on the antibacterial activity of *Rosmarinus officinalis L*., the minimum inhibitory concentration (MIC) was determined. MIC is used to evaluate antimicrobial activity of which microbial strains are susceptible and resistant to essential oil generated in the agar disc diffusion experiment. An MIC with low result suggests that less of the agent is needed to limit the organism's growth, therefore, antimicrobial agents with lower MIC scores are more effective. This MIC of *SA* was found to be 0.07 ug/mL. Meanwhile, in Bashir *et al*.'s (2020) study on *Cymbopogon citratus* (Lemon grass), the MIC of *SA* was similarly lower than that of *K. pneumoniae*, respectively, with MICs of 0.8 ug/mL and 6.25 ug/mL. Additionally, Abreu and Pino (2020) indicate that *SA* is the most sensitive bacteria to the essential oil and ethanolic extract of *P. aduncum subp. ossanum* leaves and *E. coli* isolates were shown to be more susceptible than reference strains. A higher zone of inhibition is also seen with *SA* isolates, followed by *E. coli*. Gram-positive peptidoglycan cell wall allows hydrophobic molecules to penetrate and reach the internal environment.[4] In 2018, Firmino *et al*. demonstrated the bacteriostatic and bactericidal activity of *Cinnamomum zeylanicum* and *Cinnamomum cassia* against *SA*. *C. zeylanicum* showed a bacteriostatic effect at 0.50 ug/mL and *C. cassia* had the same effect at 0.25 ug/mL.[5] With the given data above, it is proven that essential oils are an effective antibacterial agent against uropathogenic bacteria. *S. aureus* appears to be the most susceptible bacterium because of its MIC value of 0.07 ug/mL, which is approaching zero ug/mL.

The sensitivity of uropathogenic bacteria to the antibacterial agent is proportional to the diameter of the zone of inhibition. The presence of large zones of inhibition indicates sensitivity, whereas the absence of such zones or smaller zones indicates resistance. A study by Bozkurt *et al*. (2017) showed that Star Ruby grapefruit showed a high antibacterial activity against gram positive *L. monocytogenes* with a zone of inhibition of 16 mm, with Satsuma mandarin and Meyer lemon showing the least activity with 11 mm inhibition zones for both.[6] This is also similar to the antibacterial activity against *E. faecalis*, since Star Ruby grapefruit also exhibited the highest antibacterial activity with a zone of inhibition of 13 mm. For *B. cereus*, Meyer lemon shows the highest activity with 15 mm inhibition zone while Satsuma mandarin and Washington Navel orange showed the least with 10 mm. A study of the bactericidal activity of *Hemidesmus indicus* is shown to be more effective against the gram-positive *Staphylococcus aureus*.[2] The zone of inhibition of *S. aureus* in the following constituents of *H. indicus* would be 0.5 cm for petroleum benzene and acetone, 0.8 cm for chloroform, and 1.0 cm for methanol.[2]

Shanaida *et al*. (2021) used *Salvia sclarea L., Monarda didyma, Thymus pulegioides, Thymus vulgaris, and Thymus serpyllum L.* essential oils against eight gram-positive strains of bacteria. All of the essential oils tested positive for antibacterial activity against the gram-positive bacteria. The essential oils showed significant activity against the *S. pyogenes* strain, specifically *Thymus vulgaris*.[7] In a different study, Tibyangye *et al*. (2015) investigated the effectiveness of *Ocimum suave* essential oils against the clinical strain and ATCC12692 strain of *SA*. It has shown effectiveness and activity against the isolates with a mean MIC ranging from 10-20 ug/ml. When it comes to the zone of inhibition, the following uropathogens are vulnerable to essential oils, based on the data stated above: *L. monocytogenes* and *B. cereus*.[8]

Effectiveness of Essential Oils on Gram-Negative Bacteria

In a study conducted with *Syzgium aromaticum* (clove) and *Cinnamomum burmannii* (cinnamon), all essential oils were considered bactericidal against ESBL-producing *E. coli (EC)* and *K. pneumoniae (KP)*.[9] Cinnamon essential oil demonstrated a higher antibacterial effect on *EC* than clove essential oil. The growth of bacteria was inhibited by *Syzgium aromaticum* essential oil at 0.78 ug/mL. On the other hand, *Cinnamomum burmannii* was effective for both bacteria from a range of 0.39 to 1.56 ug/mL. The lowest concentration of the EOs that show no growth in subculture is referred to as the minimum inhibitory concentration (MIC).

In order to assess whether the uropathogen is susceptible or resistant to the EO, MBC values are determined. For clove and cinnamon essential oils, MBC ranges from 0.78 ug/mL to 1.56 ug/mL. The inhibition zones of clove essential oil against *EC* and *KP* range from 15.0±1.00 to 24.3±0.57 mm, and 15.6±2.08 to 25.3±0.57 mm for cinnamon essential oil. Both essential oils in the study were potentially active against *EC* and *KP*. In a similar study against *EC*, Firmino *et al*. indicated its inhibition at 0.50 ug/ml using *Cinnamomum zeylanicum*, and 0.25 ug/ml using *Cinnamomum cassia*. Antimicrobial activity of these Cinnamomum species were found against *P. aeruginosa* with an MIC value of 0.50 ug/mL.[5] Lagha *et al*. worked on the effectiveness of medicinal plants essential oils and antibacterial activity was only observed in the essential oils of *Thymus zygis*, *Origanum majorana*, and *Rosmarinus officinalis* against *EC*.[10] By disc diffusion, *T. zygis* had the highest inhibitory effect on 90% of the isolates, followed by *O. majorana* (26%) and *R. officinalis* (14%). *T. zygis* essential oil exhibited the highest antibacterial activity against *E. coli* with a range of MIC values of 0.19 ug/mL to 0.78 ug/mL, while the MBC values was reported to be in the range of 1.56 ug/mL to 6.25 ug/mL.

In the study of Wang *et al. S. aureus* and *S. marcescens* had the higher sensitivity to *M. bracteata* EO, whereas *P. aeruginosa* displayed the strongest resistance.[11] In the study of Brochot *et al*. AB1 showed the lowest MBC against *B. fragilis* (MBC: 0.01% v/v) and AB2 against *B. catarrhalis* (MBC: < 0.01% v/v).[12] There were no significant changes in sensitivity between Gram-positive and Gram-negative bacteria, which might be explained by a combined impact of the EOs or some of their components.

With 100% concentration of *Corymbia citriodora* leaves, the highest zone of inhibition of 12.1±1.9 mm was obtained with *E. coli*.[13] Moustafa *et al*. tested essential oils against *E. coli*. Clove and oregano demonstrated the most active essential oils against the uropathogenic strain ranging from 0.25 to 1 ug/ml in contrast to rosemary and cinnamon with the least inhibition.[14] Qaralleh *et al*. indicated the inhibitory effects of *Origanum ramonense* essential oil against four gram-negative isolates.[15] *EC* was a part of the most sensitive isolate against *Origanum ramonense* followed by *E. aerogenes, P. aeruginosa and K. pneumoniae* having a 20.2-24.5 mm zone of inhibition range.

Scazzocchio *et al*. (2017) investigated the effectiveness of the essential oil of *Coriandrum sativum* against two different strains of *E coli*. The essential oil was able to prevent bacterial growth of *E. coli* ECP19 and ECP32 with a MIC (mg/mL) of 6.25 for both.[16] Tibyangye *et al*. (2015) used nine strains of gram-negative bacteria against *Ocimum suave*. The essential oil was active against the gram-negative strains, specifically, the *E. coli* strains. It had no antibacterial effect on the Acinetobacter species. Shanaida *et al*. (2021) proposed essential oils of *Salvia sclarea L., Monarda didyma, Thymus pulegioides, Thymus vulgaris, and Thymus serpyllum L.* were used against four different gram-negative strains of bacteria. All of the essential oils used in the study had antibacterial activity, with a mean MIC ranging from 9 to 30. *Thymus pulegioides* and *Monarda didyma* had the most significant activity compared to the other essential oils.

Specific citrus species such as Satsuma mandarin, Clementine mandarin, Meyer lemon, Interdonato lemon, Washington Navel Orange, Star Ruby grapefruit, Sour orange, and Moro blood orange were studied by Bozkurt *et al*. (2017). Moro blood orange exhibited the strongest antibacterial activity for both gram positive and gram-negative bacteria. Its zone of inhibition against the gram-negative bacteria *EC* is 19 mm in diameter which shows the most antibacterial activity, in comparison with Interdonato lemon, Star ruby grapefruit, Satsuma Mandarin, and Meyer lemon which has a zone of inhibition of 15 mm, 14 mm, 11 mm, and 10 mm, respectively. Moro blood orange exhibited the lowest antibacterial activity against the gram-positive bacteria *B. cereus*. Moro blood orange is also the one who showed the highest activity on the other gram-negative bacteria in the study, *S. typhimurium*, with a zone of inhibition of 12 mm, Satsuma Mandarin showed the lowest activity with 7 mm, but three other species namely Sour orange, Clementine Mandarin, and Washington Navel orange exhibited no antibacterial activity against this bacteria.[6]

Ahmadian and Moghaddam (2020) used the leaves of Eryngium *caucasium Trautv* and *Froriepia subpinnata* to determine the susceptibility of 91 *E. coli* isolates. The extracts of *Eryngium caucasium Trautv* and *Froriepia subpinnata* are classified as EoEs (essential oil of Eryngium *caucasium Trautv*), EtEc (ethanolic extract of *Eryngium* c*aucasium Trautv*), AqFs (aqueous extract of *Froriepia subpinnata*), and EtFs (ethanolic extract of *Froriepia subpinnata*). Herbal products' inhibitory effects on total isolates can be classified as follows: EoFs > EtFs > EtEc > AqFs > AqEc. The study shows that EoFs is the most effective inhibitor, with a 53.8% inhibitory rate based on the MIC of the total isolates, and AqFs exhibit the lowest inhibitory activity.[17]

Al Zuhairi *et al.* (2020) assessed the effectiveness of the essential oil of *Rosmarinus Officinalis L.* against the following bacterial strains: *S. aureus, P. vulgaris, and K. pneumoniae*. The findings revealed that *Rosmarinus Officinalis L.* essential oil is most effective against *SA*, with an inhibition zone of 8.87 ± 0.50 mm and MIC of 0.07 ± 0.02 mg/m. *P. vulgaris*, on the other hand, was less sensitive to *R. officinalis L.* essential oil, with an inhibition zone of 8.6± 0.81 mm and a MIC of 0.09± 0.03 mg/mL, followed by *K. pneumoniae*, with an inhibition zone of 8.85 ± 0.61 mm and a MIC of 0.08 ± 0.03 mg/mL.[3] The results reveal the contrast between the study conducted by Prabuseenivasan *et al.* (2006) wherein *P. vulgaris* is the most sensitive bacteria to *R. officinalis L.* essential oil, and *S. aureus* as the least sensitive.

Chemical Compounds Contributing to the Effectiveness of the Essential Oil

Bozkurt *et al.* found that d-limonene is the most abundant chemical constituent among citrus species that can contribute and exhibit antibacterial effects against uropathogens. The essential oils found in the citrus species studied also include β-pinen, linalool, α-pinene, 4-terpineol, sabinene, β-myrcene, and m-cymene. Essential oils found in Moro blood orange [*C. sinensis* (L.) Osbeck] was found to have the most amount of d-limonene (93.32%), thus also exhibiting the highest antimicrobial activity in most bacterial strains, both in gram negative bacteria, such as *E. coli* and gram-positive bacteria like *L. monocytogenes*. The other citrus species with the next highest amount of limonene would be Mayer lemon (75.50%) and Interdonato lemon with the least (66.58%).[6] In addition, thymol (15.2-56.4%), carvacrol (2.8-59.6%), γ-terpinene (9.9-21.8%) and p-cymene (8.5-13.9%) were the chemical compounds present in *O. glandulosum Desf.* that contribute to its effectivity against *E. coli*.[18]

The antibacterial activity of *Syzygium aromaticum* (clove) and *Cinnamomum burmanni* (cinnamon) essential oils is attributed to eugenol and cinnamaldehyde, respectively.[9] Eugenol impairs the cell membrane integrity of *K. pneumoniae* causing its intracellular components to leak.[19] Cinnamaldehyde increases the permeability and oxidizes the cell membrane of *E. coli*.[20] Firmino *et al.* concurred to the previous study and verified the action of other *Cinnamomum* species, *C. zeylanicum* and *C. cassia*, that contain cinnamaldehyde that corresponds to 68.71% and 90.22% respectively. In the same perspective against *E. coli*, Lagha *et al.* reported that *T. zygis* contains linalool (39.7%) that contributes to the antibacterial activity of its essential oil. They enumerated the other major compounds that could account for the effect of both *T. zygis* and *O. majorana* mentioned as Terpinen-4-ol (11.7%), β-Myrcene (8.6%), and γ-Terpinene (7.6%) since these are present in both essential oils in the study.[10] The presence of 1,8-Cineole (47.7%), α-Pinene (11.7%), camphor (9.6%) in R. officinalis may explain the antibacterial activity observed.

Antibacterial activity of *Corymbia citriodora* against *Escherichia coli* was due to the presence of citronellal, citronellol, linalool, and/or 1,8-cineole.[13] With the same uropathogenic strain, Moustafa *et al. 2015* mentioned Eugenol as the main phytochemical component for *Syzygium aromaticum* and has strong antibacterial effects against *E. coli.* It prevents enzymatic action of the uropathogen causing the cell wall to deteriorate and the cells to lyse. Carvacrol, the main component of oregano essential oil, alongside terpenoids are responsible for its antibacterial and antioxidant activity with *E. coli*.[13] According to GC-MS analysis of Origanum ramonense essential oil with a similar study by Qaralleh *et al. 2018*, it was produced with a high concentration of ooxygenated monoterpenes (86.9 %) and monoterpene hydrocarbons (9.8 %). Carvacrol (84.6%), as one of the most bactericidal components against the uropathogenic strain, alongside p-cymene (4.3%) and γ-terpinene (3.3%) were the main constituents that inhibit bacterial growth.

After a GC-MS analysis in the study of Scazzocchio *et al.* (2017), the monoterpenoid linalool, representing about 70%, was the major constituent for *Coriandrum sativum* essential oil contributing to inhibiting the *E. coli* strains. In the study of Shanaida *et al.* (2021), the main components of *Thymus vulgaris* were aromatic monoterpenoid thymol, o-Cymene, and c-terpinene. For *Thymus serpyllum*, aromatic monoterpenoid thymol and Isothymol methyl ether. The major components of *Thymus pulegioides* were a-Citral and bcitral. For *Monarda didyma*, Thymol and Eucalyptol. Lastly, for *Salvia sclarea*, linalyl acetate and linalool. The mentioned major components were known to contribute to the antibacterial activity against the uropathogens.

CONCLUSION AND RECOMMENDATIONS

The aim of this study is to present a concise systematic review of the essential oils that may assist in the prevention of uropathogenic bacteria development. Antibacterial activity of such essential oils in suppressing the formation of these bacteria may be one of the answers to the developing problem of antibiotic resistance of uropathogenic bacteria, which should be regarded as a public health concern today. The reviewed studies assessed the effects of plant-based essential oils on uropathogen bacterial growth and identified the chemical constituents that play a critical role in its antibacterial capacity.

A variety of essential oils have been shown to effectively inhibit the development of uropathogens. Accordingly, the inhibition of gram-positive *S. aureus* (most sensitive to the majority of essential oils), *S. epidermidis*, *S. pyogenes*, *L. monocytogenes*, and *C. albicans*; gram-negative *E. coli*, *K. pneumoniae*, and *P. mirabilis* has been reported. Furthermore, according to available data, the major components of each essential oil contribute to the antibacterial activity against the uropathogenic bacteria. However, each case must be examined due to its difference in chemical compounds.

Since there are many journals on plant-based essential oils that have been reviewed, the authors would like to recommend that more articles on blended essential oils be sought out and identified to improve this study. This is to assess and support the arguments for the efficacy of essential oils, not just for single plant-based essential oils, but also for blended plant-based essential oils.

Emerging and re-emerging isolates of uropathogenic bacteria can be evaluated to assess whether antibacterial properties of plant-based essential oils can further be used to prevent bacterial development and invasion to promote innovating medical treatments that will eradicate prevalence and incidence of human uropathogenic infections. The current findings can be used to implement strict health protocols and investigate other plant-based oils among fellow health researchers, with the goal of supporting and expanding the scope of interest of this study.

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Authors' Contributions

AA, CD, ME, FG, SN, RN, KS, and AY designed the study and wrote the first and second drafts of the manuscript under the supervision of DB. FG constructed the abstract of the study. AA, CD, ME, FG, SN, RN, KS, and AY wrote the introduction; CD, ME, FG, SN, KS, and AY conducted the methodology containing the eligibility criteria and data extraction. AA and RN managed the literature searches. AA, CD, ME, FG, SN, RN, KS, and AY compiled the results and furthered the discussion. ME, FG, and RN wrote the conclusion and CD and SN for the recommendations to broaden the scope of interest and future directions of the study. AA and KS wrote the acknowledgements. All authors reviewed and critically drafted the final manuscript.

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