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Review Article

A Systematic Review and Meta-Analysis of Experimental Studies: Can Red Ginger be Used in the Treatment for Women Urinary Tract Infections?

Rara Sagita[1], Eighty M. Kurniawati[2]*, Zakiyatul Faizah[3]

[1]*School of Midwifery, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*
[2]*Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*
[3]*Department of Medical Biology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*

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ABSTRACT

Women are susceptible to experience Urinary Tract Infections (UTIs) throughout their lives because of the location of their reproductive organs. Treatment in UTIs is done through a pharmacological approach. Ginger is a solution in reducing complaints in health problem. The effect of giving red ginger as a treatment for urinary tract infections in women is the purpose of this study. The systematic review and meta-analysis reporting followed the PRISMA guidelines. PICOS was used in developing the research criteria. Articles published in the last 10 years, written in English, open access, and quasi-experimental research were selected from several databases. The four databases accessed were PubMed, Science Direct, Scopus, and ProQuest. *Escherichia coli* is a common cause of urinary tract infections in women. Red ginger has antimicrobial activity. The use of red ginger can be combined with other plants. The results of the meta-analysis showed that there was an effect of using red ginger on Escherichia Coli bacteria at p-value < 0.001. Red ginger can be useful in the management of urinary tract infections but it is necessary to explain further about how to process ginger properly.

***Keywords*:** Urinary tract Infections, Ginger, Therapy, Women.

Introduction

Urinary Tract Infections (UTIs) are cases that often occur in women of various ages, from adolescent to elderly, as well as certain races and ethnicities. The handling of UTIs tends to be expensive and burdensome, even though these cases occurs in women of all backgrounds regardless of socioeconomic status or education level.[1] UTIs are serious public health problem.[2] 40% of women experience UTIs in their lifetime. Adult women are 30 times more likely to develop UTIs than men. One in three women can experience first UTIs by the age of 24.[3] UTIs are mostly caused by Escherichia coli (E-coli), accounting for about 80-90% of the cases.[4] UTIs are experienced by the Indonesian population around 100 cases per 100,000 population per year and more than 100 new cases every year.[5] The incidence of UTI was found to be higher in women than in men because of the location of their reproductive organs. Women have a shorter urethra than men. Women also have urinary organs that are closer to the anus and vagina. These characteristics make it easier for microorganisms to enter the urinary tract.[6] Women can experience UTIs many times in their lives. Approximately 60% of women will experience symptoms of acute bacterial cystitis, 20-40% of women will have additional episodes and 25-50% of women will experience several episodes.[1] The economic burden and risk of treating infection is due to the high recurrence rate and increased antimicrobial resistance among uropathogens.[2] UTIs are the reason for hospital visits globally even though the disease is often overlooked.[7] Treatment of UTIs consists of pharmacological therapy and non-pharmacological therapy. Both of these therapies aim to reduce the impact of UTIs.

*Corresponding author. E mail: eighty-m-k@fk.unair.ac.id
Tel: (+62)811-3534-449

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Pharmacological therapy is the administration of drugs including antibiotics. Several errors can occur in this type of treatment such as inappropriate antibiotics, delays in treatment, and low survival rates in septic conditions.[8] In addition, the administration of antibiotics is associated with long-term health problem.[9] Therapy for UTIs can be done by using herbal plants such as ginger (*Zingiber officinale*). Ginger contains active antioxidants, namely Shagaols, Gingerols, and Zingerone. Ginger also contains flavonoids and phenolics which are used in herbal medicine and anti-inflammatory properties that can be used for women's reproductive health.[10] Red ginger is suspected to have the ability to inhibit microbial growth.[11] This ability is related to red ginger processing techniques. Analgesic activity decreased over time found in aqueous extracts of fresh red ginger and dried ginger.[12] This study aims to systematically review and analyze the effect of giving red ginger as a treatment for urinary tract infections in women.

Materials and Methods

Study design and search strategy

Systematic literature review was carried out by identifying, analyzing, and evaluating data in accordance with research questions. Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines was followed.[13] The research question was explored using the PICO framework, namely "Does red ginger have an effect as a treatment for urinary tract infections in women?". Articles were searched on several databases, namely PubMed, Science Direct, Scopus, and ProQuest. The keywords used were "ginger", "antimicrobial activity", "urinary tract infection", and "women".

Study selection and outcome measure

The inclusion criteria in this study were articles written in English, open access, published in the last 10 years, and quasi-experimental research. The exclusion criteria were review studies, comments, and cross-sectional studies.

Data extraction, abstraction, and synthesis

Microsoft Excel forms used to screen the title and/or abstract. Quality of the articles was accessed using critical appraisal tools from the

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Effective Public Health Practice Project (EPHPP). Assessment results are reported in three categories, namely strong, moderate, and weak. There are six assessment components, including bias selection, research design, confounders, blinding, data collection methods, withdrawal, and dropout. Meta-Analysis was carried out using Open Meta-Analysis Software with the steps of calculating statistical measures, calculating research variations, calculating research weights, testing heterogeneity, and modeling random effects.

Results and Discussion

181 articles were found from various databases, namely 4 articles on Scopus, 8 articles on PubMed, 7 articles on Science Direct, and 165 articles on ProQuest. 8 articles that met the inclusion and exclusion criteria were systematically reviewed. The process of selecting articles is written down in the PRISMA flowchart in Figure 1. Critical appraisal using EPHPP obtained 7 literatures with moderate values and 1 article with weak values presented in Table 1. Escherichia coli (*E. Coli*) is a common cause of UTIs in women. *E. Coli* is the main cause of urinary tract infections in women. Although pseudomonas aeruginosa is sometimes found in greater numbers than *E. Coli*, these data may come from patients with wound infections thereby causing bias in the sample.

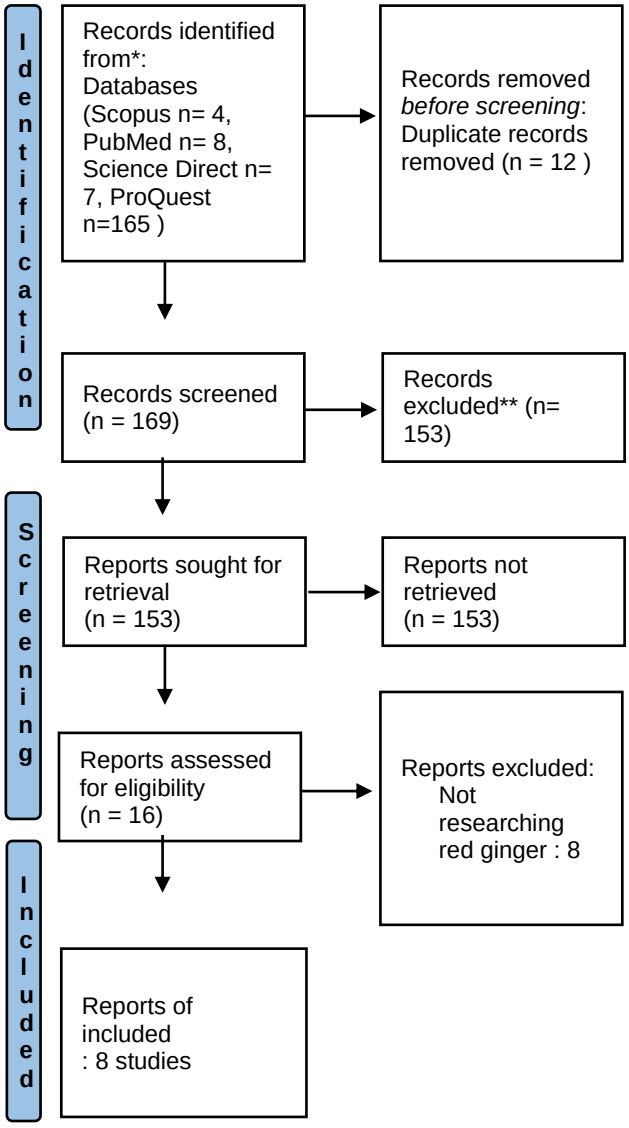

Figure 1: Prisma Flowchart

The results of the meta-analysis showed that there was an effect of using red ginger on *Escherichia Coli* bacteria as evidenced by the p-value < 0.001. It can be concluded that the results of the meta-analysis with forest plots showed that red ginger was effective in the treatment of UTIs in women. Meta-analysis was used by calculating the results of the mean ± standard deviation on the bacterial inhibition zone data. The summary results were 13,126 mm which means, strong in the bacterial inhibition zone with a confidence interval (IC 95%) i.e. (11,632-14,620). The results of the I^2 in statistical test showed a high inconsistency of 98.3%. The large I^2 value causes the use of the random effect model method. Table 3 shows the results of the heterogeneity test. Given the effect of ginger on the activity of *Escherichia Coli* which causes urinary tract infections, the treatment using ginger can be recommended for use in women. Nevertheless, the use of ginger and pharmacological therapy can be combined. This combination therapy is better than no treatment to improve the outcome of UTIs management. Ginger can serve not only as an alternative medicine but also as a companion to pharmacological therapy in treating stress and urgency of urinary incontinence.[22] This treatment aims to improve the patient's quality of life.[23] UTIs is related to the meaning of health status which refers to the analysis of the Welfare Index and is even used to estimate the quality of life experienced by adolescent girls with UTIs.[24] The effect of cases of UTIs varies depending on the socio-demographic characteristics and chronic disease of each person.[25] Gender affects the prevalence of UTIs. Women are the sex that dominates UTIs case compared to men, including adults and children.[15] 73.3% of women experiences UTIs in the vulnerable age of adolescence to adulthood. The anatomy of the urethra in women, which is about 2-3cm shorter than men, makes it easy for bacteria to contaminate the urinary tract.[20] The use of red ginger can be combined with other plants. The meta-analysis in this study could only be carried out on 3 articles, but the effect of ginger that could inhibit *E. Coli* was found in all articles that met the inclusion and exclusion criteria. The higher the concentration of red ginger, the higher the antibacterial activity obtained in ginger. When used in the form of oil, 70% of *E coli* can be inhibited by diluting ginger as much as 0.06%. These results were obtained by observing the Minimum Inhibitory Concentration test. In addition, the essential oil content in ginger of 3.9% can actually contribute to its ability to fight bacteria. The permeability of the bacterial wall can be suppressed by the presence of essential oils, nonvolite oils, and flavonoids in ginger. Microbial cell membranes are damaged by saponins and the constituent components of peptidoglycan are damaged by alkaloids.[26] A study found that antibacterial activity was not found in 2 plants, namely red ginger and juniper, but other plants such as marjoram, thymus zygis, and rosmari actually showed antibacterial activity.[18] Although, there is a study that has different results, red ginger can still be applied in improving women's health. The antimicrobial activity of red ginger has been proven to be reliable against E-coli bacteria.

Ginger can prevent various health problems. Ginger affects the prevention and treatment of diabetes mellitus when viewed from the chemical compounds found.[27] Red ginger contains compounds such as tannins, saponins, phenolics, essential oils, and flavonoids. These results are in line with other studies conducted by Tabassum *et al* (2013). They found that in addition to these substances, ginger also contains alkaloids.[20] Apart from their function, the content of red ginger with white ginger tends to be different. Red ginger has higher levels of linalool, borneol, zingiberene, and zingerone content with a significant difference compared to white ginger.[28] This study has limitations, namely the number of articles reviewed is limited and there is no regional distribution. In addition, the ability of researchers to process critical judgments affects understanding and interpretation in analyzing data.

Conclusion

Red ginger can be useful in the management of urinary tract infections in women because it has antimicrobial activity.

Conflict of Interest

The authors declare no conflict of interest.

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Table 1: Critical appraisal results

Author	Bias selection	Study design	Confounders	Blinding	Data collection method	Withdrawal and dropout	Rating
Mohamad, 2019 [14]	2	1	1	3	1	1	Moderate
Lagha, 2019 [15]	2	1	1	3	1	1	Moderate
Mohammed, 2019 [16]	2	1	1	3	1	3	Weak
Kumar, 2018 [17]	2	1	1	3	1	1	Moderate
Al-Zamily, 2017 [18]	2	1	1	3	1	1	Moderate
Mourad et al, 2016 [19]	1	1	2	3	1	2	Moderate
Tabassum, 2013 [20]	2	1	1	3	1	2	Moderate
O. Al-Jiffri, 2011 [21]	2	1	1	3	1	1	Moderate

Table 2: Characteristics of studies exploring the use of ginger in UTIs in women

Author, year	Country	Research type	Sample setting	Type of ginger	Bacteria type	Finding
Mohamad, 2019 [14]	Iraq	Quasi-experimental study	50 samples of urine from patients (male and female) suffering from UTIs.	Alcoholic extraction of *Zingiber officinale*	*Escherichia Coli*	Ginger alcohol extract had an antimicrobial effect in UTIs case and no side effects were found.
, 2019 [15]Lagha	Saudi Arabia	Quasi-experimental study	50 patients 35 women and 15 men	5 medicinal plant essential oils are Origanum majorana, Thymus zygis, Rosmarinus officinalis, Juniperus communis and Zingiber officinale.	*Escherichia Coli*	*Zingiber officinale* did not show any antimicrobial effect against Escherichia coli isolates.
Mohammed, 2019 [16]	Iraq	Quasi-experimental study	35 samples were collected from patients with UTIs and wound infections.	Ginger extracts	*Escherichia coli*, Pseudomonas aeruginosa, Klebsiella pneumonae *and* *Staphylococcus aureus*	The antibacterial activity of Ginger against Escherichia coli was indicated by an inhibition zone of 15-19mm.
Kumar, 2018 [17]	Thailand	Quasi-experimental study	20 urine of UTI patient	Ginger oil	*Escherichia Coli*	Ginger oil was found to have antibacterial activity against clinical isolates of E. coli.
Al-Zamily, 2017 [18]	Dubai	Quasi-experimental study	63 clinical urine samples	Aqueous extract of ginger	*Escherichia Coli*, P. mirabilis and K. pneumoniae	The use of aqueous extracts of ginger (50% and 100%) showed an antimicrobial effect on the growth of isolated bacteria.
Mourad et al, 2016 [19]	Cairo	Quasi-experimental study	1600 urine of UTI patient	15 plants were extracted by boiled water, ethanol or tested as essential oils, highest antibacterial activity was exhibited by	*Staphylococcus aureus*, *Escherichia coli*, Pseudomonas aeruginosa, Enterococcus	Red ginger has antibacterial activity against Escherichia Coli

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				essential oils plant extracts	faecalis, Klebsiella pneumoniae	
Tabassum, 2013 [20]	India	Quasi-experimental study	200 urine samples	6 plants (Coriander sativum, Syzygium aromaticum, Cinnamomum cassia, Zingiber of icinale, Terminalia chebula, and Azadirachta indica) and their parts (leaves, bark, flower, rhizome, and fruit) with ethanolic extracts	*Escherichia coli* (44%); Klebsiella pneumoniae (25.33%); Pseudomonas aeruginosa (20%); Enterobacter faecalis (6.66%) and Proteus mirabilis (4%)	The five isolates showed broad-spectrum antibacterial activity and were higher than the ten standard antibiotics.
O. Al-Jiffri, 2011 [21]	Saudi Arabia	Quasi-experimental study	130 urine samples	Ginger (dry, fresh)	*Escherichia coli*	The effect of antibacterial activity by red ginger against *Escherichia coli* showed that the MIC of ginger was 50%.

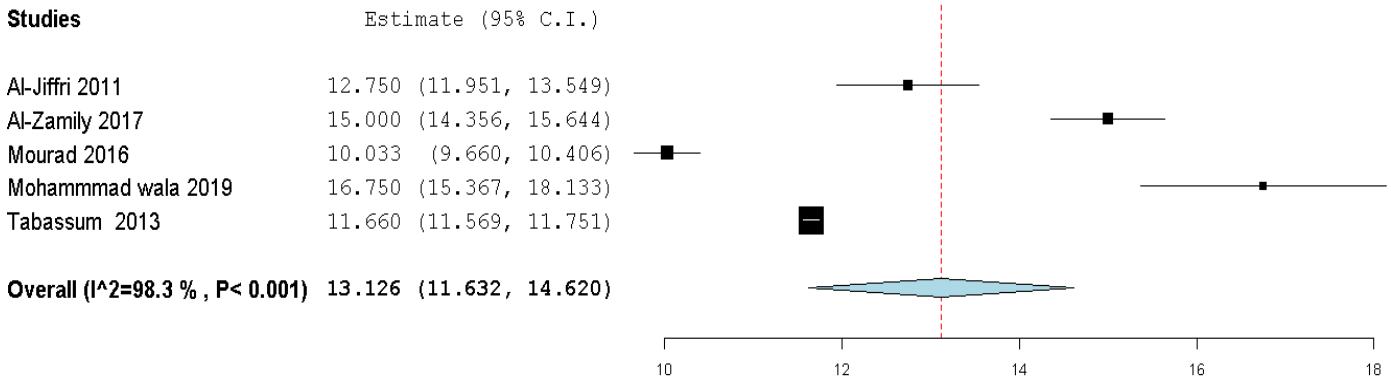

Figure 2: Forest plot

Table 3: Test for heterogeneity

T^2	Q(df = 4)	Het. P-value	I^2
2.754	235.356	< 0.001	98.3

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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