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Antioxidant and Antibacterial Activity of Centella asiatica Herb Extract on Escherichia coli Using Ethanol Solvent at Various Concentrations

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Abstract **Original Research Article**

This study explores the antioxidant and antibacterial activity of Centella asiatica herb extract with the aim of identifying the optimal extraction method to maximize its biological potential. Given the increasing bacterial resistance to antibiotics and the need for safer natural alternatives, this research focuses on using ethanol as a solvent at various concentrations for the extraction of bioactive compounds. The research methodology involves extraction with 25%, 50%, and 75% ethanol, followed by the evaluation of antioxidant and antibacterial activity against Escherichia coli. The results indicate that ethanol concentration in Centella asiatica extract significantly affects its antioxidant and antibacterial potential. The 75% ethanol extract exhibited the highest antioxidant and antibacterial activity, with significant differences observed in the ANOVA test (p-value 0.000). The study concludes that the 75% ethanol extract of Centella asiatica possesses high therapeutic potential, with higher extract concentrations yielding stronger antioxidant and antibacterial effects.

Keywords: Centella asiatica, antioxidant, antibacterial, antibiotic resistance, oxidative stress, extraction method, herbal medicine.

INTRODUCTION

Antioxidant and antibacterial activities are key aspects of research in health and pharmacology, particularly in the development of herbal medicines (Malahayati *et al*., 2021). Centella asiatica herb is widely recognized for its therapeutic potential, including its antioxidant and antibacterial activities. With the rising bacterial resistance to conventional antibiotics, there is an urgent need for safer and more effective natural solutions (Thepthong *et al*., 2023). This research aims to determine the most effective extraction method for Centella asiatica using ethanol as a solvent at various concentrations to maximize its biological potential and contribute to the development of more effective herbal medicines (El Mannoubi, 2023).

The increasing cases of antibiotic resistance pose a serious global health threat (Assiry *et al*., 2023). This resistance not only increases morbidity and mortality but also adds economic burdens to healthcare systems (Ahmed *et al.*, 2022). Additionally, oxidative stress caused by free radicals contributes to various chronic diseases such as cancer, diabetes, and heart disease (Audah *et al*., 2022). This study focuses on the antioxidant and antibacterial potential of Centella asiatica extract as an alternative solution that can help mitigate oxidative stress and combat bacterial infections (Nguyen *et al*., 2020).

The selection of variables in this study is based on the synergistic potential of the antioxidant and antibacterial activities of Centella asiatica, which may offer more comprehensive health benefits (Shalaby *et al*., 2023). The use of ethanol solvent at various concentrations aims to identify the most effective solvent for extracting active compounds, thereby enhancing the efficiency and therapeutic potential of the extract (Zreen *et al.*, 2022). The advantage of this approach lies in its ability to optimize the extraction of bioactive compounds, thereby maximizing health benefits and reducing the potential side effects associated with synthetic chemicals (Jirakitticharoen *et al*., 2022).

This study also focuses on the antioxidant capacity of Centella asiatica extract to neutralize free radicals and prevent cell damage caused by oxidation, as well as its antibacterial ability to inhibit the growth of Escherichia coli (Pontes *et al.*, 2022). While the potential of Centella asiatica as a natural antioxidant source is

well-known, further research is needed to explore its antibacterial activity against various bacterial strains (Majhi *et al*., 2023). The uniqueness of this research lies in its comprehensive approach, combining the analysis of antioxidant and antibacterial activities with the use of various ethanol solvent concentrations. The primary objective of this study is to identify the most effective extraction method to maximize the therapeutic potential of Centella asiatica, which could contribute to addressing global health challenges, particularly antibiotic resistance and oxidative stress-related diseases (Li *et al*., 2023).

This research is expected to provide new insights into the utilization of Centella asiatica as an effective source of antioxidants and antibacterial agents, as well as to contribute to the development of better and more sustainable health strategies (Saptowo *et al.*, 2022). The results of this study are anticipated to encourage the use of Centella asiatica in herbal medicine formulations and support global efforts to tackle health issues related to antibiotic resistance and oxidative stress.

Theoretical Framework

Antioxidant Activity in Centella asiatica Extract

Antioxidants are compounds that can neutralize free radicals, which are molecules with unpaired electrons and highly reactive to biological structures. These free radicals play a role in the aging process and various degenerative diseases such as cancer, diabetes, and heart disease. Centella asiatica contains phenolic compounds, flavonoids, and triterpenoids known for their significant antioxidant capabilities. These compounds work by donating electrons to neutralize free radicals, thereby preventing oxidative damage to body cells (Prayitno & Rahim, 2020). Previous research has shown that Centella asiatica extract exhibits strong antioxidant activity when extracted with ethanol, which is higher compared to water as a solvent. Another study found that the antibacterial activity of Centella asiatica is more effective against Gram-positive bacteria compared to Gram-negative bacteria, likely due to differences in bacterial cell wall structures (Adnan *et al.*, 2020). However, further research is needed to comprehensively explore the impact of various solvents on the biological activity of Centella asiatica extract.

Antioxidant Mechanism of Centella asiatica Herb

Antioxidant compounds in Centella asiatica, such as asiatic acid and madecassic acid, exhibit antioxidant activity through prevention, termination, and repair mechanisms of oxidative damage. As a preventive measure, these antioxidants can inhibit the formation of free radicals by binding transition metals involved in oxidative reactions. Additionally, they act as inhibitors by breaking the chain of ongoing oxidation reactions. Previous studies have shown that Centella asiatica extract can enhance the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT), which play a crucial role in detoxifying free radicals (Mehmood *et al*., 2022).

Escherichia coli Bacteria

Escherichia coli (E. coli) is a type of Gram-negative, rod-shaped bacteria and a member of the Enterobacteriaceae family. This bacterium is commonly found in the digestive tracts of humans and warm-blooded animals, where most E. coli strains are commensal and harmless. However, some strains of E. coli are pathogenic and can cause various diseases, ranging from urinary tract infections to gastroenteritis, often associated with the consumption of contaminated food or water. E. coli is known for its adaptability and can survive in various environments, both inside and outside the host's body. This bacterium is also frequently used as a model organism in molecular biology and biotechnology research due to its rapid growth and ease of genetic manipulation (Ökmen *et al*., 2023).

Antibacterial Activity in Centella asiatica Extract

In addition to its antioxidant activity, Centella asiatica is also known for its effective antibacterial properties. Compounds such as asiaticoside, madecassoside, and asiatic acid in Centella asiatica have been reported to inhibit the growth of pathogenic bacteria, including both Gram-positive and Gram-negative bacteria (Iwansyah *et al*., 2021). This antibacterial activity works through a mechanism of disrupting the bacterial cell membrane integrity, leading to leakage of cell contents and ultimately causing bacterial death (Sinaga *et al*., 2022).

The Role of Solvents in the Extraction of Active Compounds

Solvents play a crucial role in the extraction process of active compounds from plants. Different solvents have different polarities, which will affect the type and amount of compounds that can be extracted. For example, polar solvents like ethanol and methanol are more effective in extracting polar compounds such as phenolics and flavonoids, while non-polar solvents like hexane are more suitable for extracting lipophilic compounds such as essential oils. In the context of Centella asiatica, the use of various solvents can produce extracts with different compound compositions, which in turn can influence their antioxidant and antibacterial activities (Murugesan *et al*., 2021).

RESEARCH METHODOLOGY

Research Design

This study employed an exploratory experimental research design conducted at the Microbiology Laboratory of the Department of Pharmaceutical and Food Analysis, Jakarta 2 Health Polytechnic, Ministry of Health. The initial stage of the research involved the extraction process, followed by testing the antioxidant and antibacterial activities of Centella asiatica.

Tools and Materials

The tools used in this study included a macerator, glassware, clamps and stands, tripod, magnetic stirrer, wooden clamp, test tube rack, mortar and pestle, water bath, Bunsen burner, pH stick, filler, vortex mixer, cuvettes, and a UV-Vis spectrophotometer. The materials used were Centella asiatica (L.) obtained from the Bogor area in West Java, ethanol, distilled water, HPMC (Hydroxypropyl Methylcellulose), and glycerin.

Research Procedure

The sample used in this study was serum with the active ingredient of Centella asiatica (L.) extract, sourced from the Bogor area, West Java, through purposive sampling. The selection criteria included leaves that were still green and free from damage such as yellowing or drying. The herb was botanically identified at BRIN Cibinong to ensure the authenticity of the specimen.

Table 1: Research Variables

Independent Variable	Pegagan extract concentration of 75%, 50%, and 25% in ethanol solvent
Dependent Variable	Value of antioxidant activity test of pegagan extract in various solvent concentrations
	Antibacterial activity of pegagan extract in various concentrations of ethanol solvent

Maceration Extraction Method

The Centella asiatica was washed with running water and air-dried naturally. The dried herb was then crushed and sieved to obtain a homogeneous simplicia, which was microscopically identified and tested for ash content and moisture loss. The extraction process was conducted using ethanol as the solvent in three different concentrations: 75%, 50%, and 25%. Distilled water (Aquades) was used as the control solvent. The maceration method was followed by solvent evaporation using a rotary evaporator.

Antioxidant Activity Test

The antioxidant activity of the extract was tested using the DPPH method. Test solutions and control solutions were taken at 1 mL from each concentration (75%, 50%, and 25%), pipetted into test tubes, and then mixed with 1.5 mL of 40 ppm DPPH solution. The mixture was shaken until homogeneous and incubated for 30 minutes in a light-protected area. The absorbance was then read at the maximum wavelength of 515 nm (Purgiyanti, 2016). The color change of the solution was observed as an indicator of antioxidant activity.

Antibacterial Activity Test Against E. coli

The antibacterial test was performed using the diffusion method. Thick agar plates were prepared from MHA media with a thickness of 3 mm in sterile petri dishes. A sterile cotton swab was dipped into the prepared bacterial suspension, pressed against the tube's wall, and streaked evenly over the Mueller Hinton Agar media. Wells were created in the media using a boor prop, with one well for the positive control, another for the negative control, and the remaining wells for the extract at concentrations of 75%, 50%, and 25%. The plates were incubated for 24 hours at 37°C. The presence or absence of an inhibitory zone, measured in millimeters, was compared to the positive and negative controls.

Data Analysis

The data were analyzed quantitatively using the Kolmogorov-Smirnov test to determine data distribution, One-Way ANOVA for variance analysis, and the LSD test to identify differences in inhibition zones between the concentrations that could inhibit bacterial growth.

RESULTS AND DISCUSSION

Analysis of Antioxidant Activity Determination

The analysis of antioxidant activity determination was obtained by measuring the antioxidant activity in mgQE/gram, which represents the amount of antioxidant activity in the sample equivalent to a certain amount of quercetin per gram of the sample. A higher mgQE/gram value indicates that the sample has higher antioxidant activity.

Table 2: Antioxidant Activity Measurement Results (mgQE/gram)

Treatment	Repetition			Average	Stdev
	I	II	III		
75%	45.23	47.55	46.34	46.37	0.95
50%	40.21	39.77	38.23	39.40	0.85
25%	37.34	38.11	37.22	37.56	0.39
Aquades	21.55	24.23	24.66	23.48	1.38

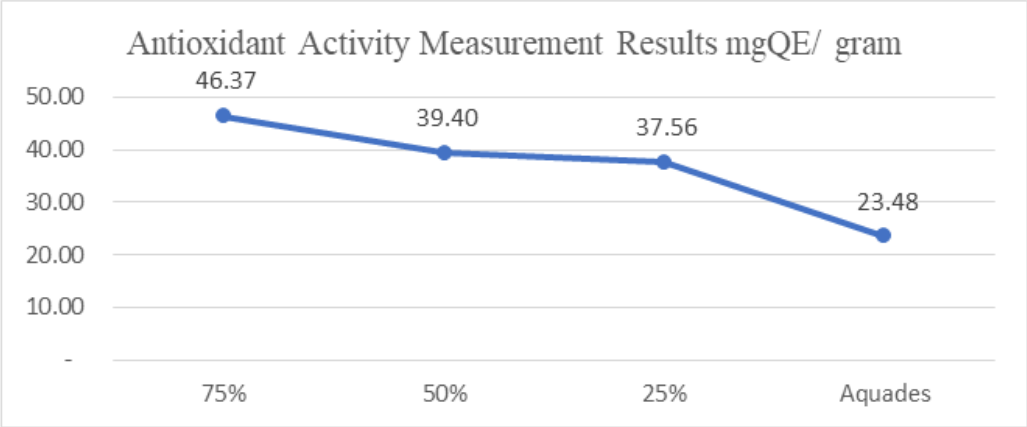

Figure 1: Results of Antioxidant Activity Measurement mgQE/gram

Analysis of Antioxidant Activity Determination

The analysis of antioxidant activity across different solvent treatments reveals a clear trend in the effectiveness of extraction based on solvent concentration. The 75% extract concentration demonstrated the highest antioxidant activity, averaging 46.37 mgQE/gram. This finding is consistent with existing literature that emphasizes the role of solvent concentration in the extraction of bioactive compounds, particularly antioxidants (Syed *et al*., 2020) . As the concentration of the extract decreased to 50% and then to 25%, the antioxidant activity correspondingly declined to 39.40 mgQE/gram and 37.56 mgQE/gram, respectively. This trend suggests that higher solvent concentrations facilitate the extraction of phenolic compounds, which are known for their antioxidant properties (Ameliana *et al*., 2022).

The lowest antioxidant activity was recorded in the Aquades treatment, with an average value of 23.48 mgQE/gram. This significant reduction in antioxidant activity when using water as a solvent aligns with findings that indicate polar solvents, such as ethanol and acetone, are more effective in extracting phenolic compounds compared to less polar solvents like water (Santos *et al*., 2021). The presence of these phenolic compounds is crucial, as they serve as primary antioxidants, scavenging free radicals and thereby mitigating oxidative stress (Aguilar-Villalva *et al*., 2021).

Moreover, the results underscore the importance of solvent choice in the extraction process. Studies have shown that different solvents yield varying levels of total phenolic content (TPC) and total flavonoid content (TFC), which directly correlate with antioxidant activity (Aguilar-Villalva *et al*., 2021). For instance, demonstrated that acetone and ethanol extracts exhibited higher antioxidant activities compared to methanol and water extracts, reinforcing the notion that solvent polarity significantly influences the extraction efficiency of antioxidant compounds (Ferreira-Santos *et al*., 2020). In summary, the data presented indicate a clear relationship between solvent concentration and antioxidant activity, with higher concentrations leading to enhanced extraction of beneficial compounds. This finding is critical for optimizing extraction methods in order to maximize the antioxidant potential of plant materials, which can have significant implications for food science and health-related applications.

The graph demonstrates consistency in measurement results across repetitions, with relatively low standard deviation values for each treatment (e.g., 0.85 for the 50% treatment and 0.39 for the 25% treatment). This indicates that antioxidant activity measurements were performed with a good level of precision. From these results, it can be concluded that higher concentration solvents (75%) are more effective in extracting compounds with antioxidant activity compared to more diluted solvents like Aquades.

Analysis of Antibacterial Activity Determination

The antibacterial activity test results of Centella asiatica leaf extract against E. coli were conducted using the diffusion method. The extracts were prepared in three concentrations: 75%, 50%, and 25%. The control variable used was Aquades.

Table 3: Test Results of Centella Asiatica Extract Against E. coli Using the Diffusion Method

Treatment	Repetition			Average	Stdev
	I	II	III		
75%	13.23	14.22	14.21	13.89	0.46
50%	13.21	12.33	14.22	13.25	0.77
25%	10.44	11.21	10.99	10.88	0.32
Aquades	2.11	1.29	0.89	1.43	0.51

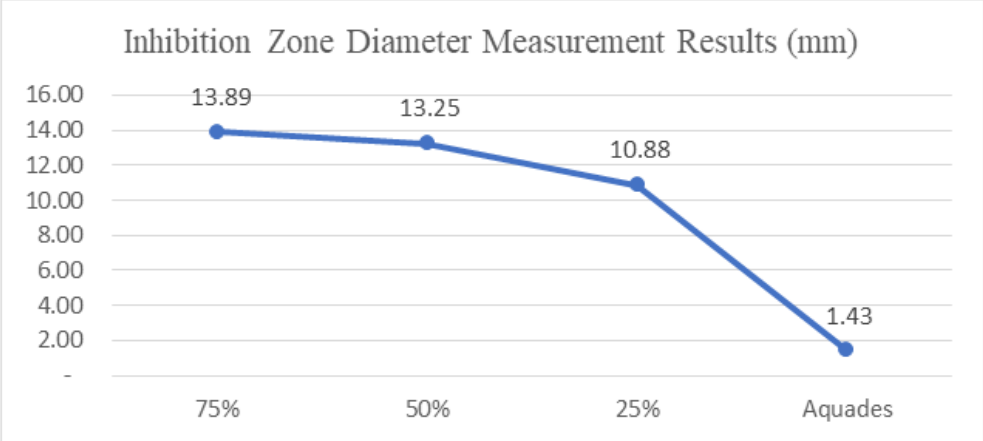

Figure 2: Relationship between the concentration of pegagan extract and the growth inhibition zone of E.Coli bacteria

Based on the provided data, the analysis of antibacterial activity determination shows a positive relationship between the concentration of Centella asiatica extract and the inhibition zone of E. coli growth.

The antibacterial activity of Centella asiatica extract against Escherichia coli (E. coli) has been shown to be concentration-dependent, as evidenced by the observed inhibition zones at varying extract concentrations. At a 75% extract concentration, the average inhibition zone was recorded at 13.89 mm, which is the largest among the tested concentrations. This finding aligns with previous studies that indicate a positive correlation between extract concentration and antibacterial efficacy (Adibuduge & Senevirathne, 2023). Specifically, the results suggest that higher concentrations of Centella asiatica extract are more effective in inhibiting the growth of E. coli, which is consistent with the general understanding of plant extracts' antibacterial properties ("Evaluation of the Efficacies of Selected Medicinal Plants on Pathogenic Escherichia Coli Strains", 2016).

As the concentration of the extract decreases, the inhibition zone also diminishes. At a 50% concentration, the average inhibition zone was 13.25 mm, and at a 25% concentration, it further decreased to 10.88 mm. This trend is supported by the literature, which indicates that lower concentrations of plant extracts typically yield smaller inhibition zones due to insufficient active compounds to exert a significant antibacterial effect (Adibuduge & Senevirathne, 2023). Furthermore, the treatment with Aquades, which served as a control without the extract, resulted in an average inhibition zone of only 1.43 mm, indicating minimal antibacterial activity. This finding underscores the necessity of the active compounds present in Centella asiatica for effective antibacterial action against E. coli (Feng *et al*., 2022). The concentration-dependent nature of the antibacterial activity of Centella asiatica against E. coli is further corroborated by studies that demonstrate similar patterns in other plant extracts.

For instance, extracts from various medicinal plants have shown that higher concentrations correlate with larger inhibition zones against E. coli and other pathogenic bacteria (Tsvetov *et al*., 2023). The active compounds in these extracts, such as flavonoids and saponins, are believed to disrupt bacterial cell walls and inhibit essential cellular processes, thereby enhancing their antibacterial efficacy. In summary, the results of this study reinforce the notion that the antibacterial activity of Centella asiatica extract against E. coli is significantly influenced by the concentration of the extract used. Higher concentrations lead to larger inhibition zones, indicating stronger antibacterial activity, while lower concentrations result in diminished effectiveness. This concentration-dependent relationship is a critical consideration for the application of plant extracts in combating bacterial infections.

ANOVA					
Anti_Bakteri					
	Sum of Squares	**df**	**Mean Square**	**F**	**Sig.**
Between Groups	299.502	3	99.834	226.642	.000
Within Groups	3.524	8	.440		
Total	303.026	11			
Anti_Oksidan					
Between Groups	829.151	3	276.384	200.988	.000
Within Groups	11.001	8	1.375		
Total	840.152	11			

To determine significant differences between each concentration, the data was statistically analyzed using a one-way ANOVA test. Both tables display the results of the ANOVA test for each category (Antibacterial and Antioxidant). In both analyses, a high F-value and a significant Sig. value ($p < 0.05$) indicate that the differences between treatment groups are statistically significant for both tests. The results of both ANOVA tests show that variations in Centella asiatica extract concentration significantly affect both antibacterial and antioxidant activities.

CONCLUSION

The antioxidant activity test showed that the concentration of Centella asiatica extract significantly influences the antioxidant potential measured in mgQE/gram. The 75% extract concentration produced the highest antioxidant activity (mgQE/gram), as well as the largest inhibition zone in the antibacterial test against E. coli. This activity decreases with lower extract concentrations (50% and 25%), with Aquades as the control showing the lowest effect. The ANOVA test revealed highly significant differences between the various extract concentrations, with a high F-value and a very low p-value (0.000). Higher concentrations of Centella asiatica extract provided stronger antioxidant and antibacterial effects.

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