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Phytochemical Screening and Antioxidant Activity of the *Centella asiatica* Leaf Extracts In a Variety of Solvents

Erlin Saalino[1)], Halifah Pagarra [2)*]

[1)2)]Universitas Negeri Makassar, Indonesia

Correspondence E-mail: halifah.pagarra@unm.ac.id

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Abstract

Centella asiatica is a type of herbaceous plant that has many health benefits. This plant is a source of phenolic compounds, flavonoids, triterpenoids, alkaloids and tannins. This research aims to examine the phytochemical content and antioxidant potential of 70% ethanol extract of *Centella asiatica* leaf and the results of fractionation using 3 types of solvents with different polarities. *Centella asiatica* leaves were extracted by maceration method, then fractionation and phytochemical screening were carried out. The total phenolic content test was carried out using the Folin Ciocalteu method and the antioxidant activity test was carried out using the DPPH (2,2-diphenyl-1-picrylhydrazyl) method. The yield of 70% ethanol solvent maceration, n-hexane fraction, ethyl acetate fraction and methanol fraction were 18.782%, 3.05%, 6.19%, and 92.46%, respectively. Phytochemical screening of 70% ethanol extract of *Centella asiatica* leaves contains flavonoids, tannins, phenolics, alkaloids and steroids. The n-hexane fraction contains alkaloids, tannins, phenolics and triterpenoids. The ethyl acetate fraction contains flavonoids, saponins, tannins, phenolics, alkaloids and steroids. The methanol:water fraction contains alkaloids, flavonoids, saponins, tannins, phenolics and triterpenoids. The total phenolic content test of 70% ethanol extract, n-hexane fraction, ethyl acetate fraction and methanol:water fraction was 12.773 ± 0.479 mg GAE/g, 1.182 ± 0.124 mg GAE/g, 18.334 ± 0.305 mg GAE/g, and 10.211 ± 0.247 mgGAE/g, respectively. Antioxidant activity of 70% ethanol extract, n-hexane fraction, ethyl acetate fraction and methanol:water fraction with IC50 values of 7.4 ppm, 2122.5 ppm, 45.6 ppm and 126 ppm..

Keywords: Antioxidants, *Centella asiatica*, *Extraction, Fractionation, Phytochemicals*.

INTRODUCTION

Synthetic and chemical-based drugs are usually associated with bad side effects. Therefore, plant-based medicine is gaining interest because of its natural and environmentally friendly characteristics with fewer side effects (Jahan et al., 2022). In the process of drug discovery, secondary metabolites from plants can be used as complementary materials for chemically synthesized compounds, because they are better in terms of biological and pharmacological activity. The content of secondary metabolites in plants is very complex, so it is necessary to carry out phytochemical screening before conducting more in-depth research on these natural ingredients. Phytochemical screening is an important effort in discovering natural ingredients that have potential as medicines (Chauhan et al., 2020).

Free radicals are thought to trigger many serious diseases (Anam et al., 2023). Free radicals are capable of damaging many cellular components such as proteins, lipids and DNA. Currently, there is an increasing interest in the biochemical and pharmacological functions of natural antioxidants from vegetables, fruits, and medicinal plants, which may be candidates for

preventing oxidative damage, hence promoting health (Arora et al., 2018). Increasing amounts of free radicals can cause dangerous physiological responses that can cause cell damage and various diseases such as diabetes, carcinogenesis, and inflammation (Melaku & Worku, 2020; Zhazykbayeva et al., 2020). Phytochemical compounds from plant extracts including phenolics and flavonoids are known to play a role because of their antioxidant properties (Barghout et al., 2020; de Oliveira et al., 2019; Tanleque-Alberto et al., 2020). This is the reason for finding new antioxidant and therapeutic agents from natural sources because they are thought to have antioxidant properties.

Centella asiatica is a medicinal plant of the Apiaceae family which has long been used in traditional medicine, because it has antibacterial, antiviral, anti-hypertensive, diuretic and anti-inflammatory properties (Waluyo, 2021). This plant grows a lot in rice fields, plantations, fields and roadsides (Manganti, 2021). *Centella asiatica* is a promising source of essential oils, triterpenoids and phenolic compounds, especially flavonoids which contribute to antimicrobial and antioxidant properties. The leaves and roots are used to treat various symptoms and ailments caused by bacterial infections (Wong & Ramli, 2021). The most well-known active compounds in *Centella asiatica* are asiaticoside, madecassoside, asiatic acid and madecassic acid. These compounds can alleviate inflammation, act as antioxidants and promote collagen synthesis (Waluyo, 2021). Asiaticoside is the primary compound known for its anti-inflammatory and antioxidant effects, as well as its ability to repair damaged skin tissue (Saras, 2023). Gotu Kola contains asiaticoside which has antibacterial activity, triterpenoids, tannins, alkaloids, glycosides and flavonoids (Rahmat, 2022).

Therefore, in this research, fractionation of 70% ethanol extract was carried out with 3 types of solvents with different polarities, namely n-hexane (non-polar), ethyl acetate (semi-polar) and methanol (polar). This aims to determine the yield results, differences in phytochemical content, total phenolic content and the best antioxidant activity.

RESEARCH METHODS

Raw Material Preparation

The main raw material used in this research was *Centella asiatica* leaves from the Masamba area in North Luwu Regency. *Centella asiatica* leaves were air dried at room temperature and then ground using a blender until they form a powder. *Centella asiatica* leave powder was sieved using a 60-mesh.

Extraction Procedure

Samples that had been mashed in powder form were weighed as much as 500 gr and then macerated using 70% ethanol as much as 5000 mL for 24 hours (remaceration of 3 times with the same solvent). Furthermore, the filtrate was evaporated using a rotary evaporator at 40oC until a thick extract was obtained (Halifah et al., 2019). The extract obtained was calculated using the formula:

$$\text{The Yield} = \frac{weight\ of\ fraction\ (gr)}{weight\ of\ extract\ (gr)}\ x\ 100\ \%$$

Fractionation

Fractionation used 3 types of solvents, namely, n-hexane, ethyl acetate and methanol. The thick extract was weighed as much as 20 gr then dissolved in 100 ml of distilled water which had been heated first. The mixture was put into a separating funnel and then 100 ml of n-hexane was added. Two phases were formed, namely the water phase at the bottom and the n-hexane phase at the top, then the two phases were separated. The fractionation was repeated 5 times

with n-hexane (FH). Further fractionation in the same way using ethyl acetate (FEA) and methanol (FMA) solvents (Ahmad et al., 2021). The fractionation results obtained were calculated using the formula:

$$\text{The Yield} = \frac{weight\ of\ fraction\ (gr)}{weight\ of\ extract\ (gr)}\ x\ 100\ \%$$

Phytochemical Screening

Analysis of active compound content follows the Harborner 1987 method. Analysis of active compound content includes alkaloid test, saponin test, tannin test, phenolic test, flavonoid test, steroid and triterpenoid test.

A positive result of the alkaloid test in Mayer's reagent is a white precipitate and in Dragendorff's reagent there is a red or orange precipitate. Positive results of the saponin test formed stable foam for ± 7 minutes. Positive tannin test results show a green, blue or black color. Positive results of the phenolic test show green, red, purple, blue or black. Positive results of the flavonoid test show a red, yellow or orange color. Positive results of the steroid test show a purple, blue or green color and the triterpenoid test shows a red or brown color.

Determination of Phenolic Content

Phenolic compounds are the largest group of compounds that act as natural antioxidants in plants. Determination of total phenolic using the Folin Ciocalteu method. A total of 10 mg of the extract was dissolved in 10 ml methanol (1000 ppm). A total of 0.2 ml of 1000 ppm concentration was taken and added with 15.8 ml of distilled water. Folin Ciocalteu reagent were added as much as 1 ml and allowed to stand for 7 minutes at room temperature. Three ml of 10% Na2CO3 was added and incubated for 30 minutes at room temperature. The absorbance was calculated using a uv-vis spectrophotometer at a wavelength of 765 nm and replicated 3 times (Hartati et al. 2022).

Antioxidant Activity

Antioxidant activity test was carried out using the DPPH (2,2-diphenyl-1-picrylhydrazyl) method. A total of 5 mg of DPPH as a blank was dissolved in 100 ml methanol (50 ppm). A total of 3 ml of blank was incubated for 30 minutes in a dark room, the absorbance was measured at a wavelength of 517 nm (3 times of replication). Vitamin C 1 mg was dissolved in 10 ml methanol (100 ppm) and prepared in concentrations of 2, 4, 6, 8 and 10 ppm. Take 77 µl of each concentration and add 3 ml of DPPH solution. The vitamin C solution was incubated for 30 minutes in a dark room and the absorbance was measured at a wavelength of 517 nm (3 times of replication).

A total of 5 mg of the extract was dissolved in 10 ml of methanol (500 ppm) and prepared in concentrations of 10, 50, 100, 150 and 200 ppm. Take 77 µl of each concentration and add 3 ml of DPPH solution. The solution was incubated for 30 minutes in a dark room and the absorbance was measured at a wavelength of 517 nm (3 times of replication) (Hartati et al. 2022).

Statistical Analysis

Data were analyzed by ANOVA ($\alpha = 0.05$). Further tests with the Tukey test method were carried out to determine the significance between the extract and fraction treatments. Significance is based on a P value < 0.05.

RESULTS AND DISCUSSION

Centella asiatica leaf samples were extracted and fractionated with different solvents to see how much yield was obtained in each solvent. Yield is the comparison between the weight of the extract obtained and the weight of the simplicia. The greater the yield percentage, the greater the amount of extract obtained (Nahor, Rumagit, and Tou 2020). The rendition results are presented in Figure 1.

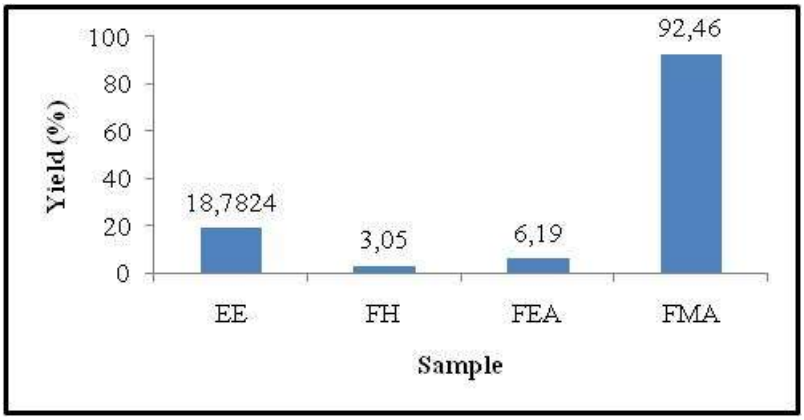

Figure 1. Yield of *Centella asiatica* Leaves

Figure 1 showed that the fraction with methanol:water (FMA) solvent obtained the highest yield namely 92.46%, then the extract with 70% ethanol solvent (EE) with 18.7824% yield, 6.19% ethyl acetate (FEA) solvent, and n-hexane (FH) 3.05%. These results indicate that the methanol solvent is better at attracting the chemical components in the extract. This may be influenced by the polarity of the chemical components in the extract, which are more polar in nature.

Table 1. Phytochemical Screening of *Centella asiatica* Leaves

Phytochemical Screening	Sample			
	Ethanol Extract 70%	n-Hexane Fraction	Ethyl Acetate Fraction	Methanol:Water Fraction
Alkaloids				
Mayer	+	-	-	+
Dragendorff	+	+	+	+
Flavonoids	+	-	+	+
Saponins	-	-	+	+
Tannins	+	+	+	+
Phenolic	+	+	+	+
Steroids	+	-	+	-
Triterpenoids	-	+	-	+

Note : (+) Detected; (-) Not Detected

The results of the phytochemical analysis are presented in Table 1. The result of the tests revealed that the methanol:water fraction, followed by the ethyl acetate fraction and ethanol extract identified more secondary metabolite compounds than the n-hexane fraction. The secondary metabolites identified were flavonoids, alkaloids, saponins, tannins, phenolics, steroids and triterpenoids. Several groups of secondary metabolites have the potential to act as antioxidants, namely phenolics and flavonoids. These results are also supported by several studies that *Centella asiatica* contains alkaloids, phenolics, flavonoids, saponins, tannins, triterpenoids, steroids and glycosides (Pokhrel & Neupane, 2021; Sieberi et al., 2020; (Vinolina & Sigalingging, 2021). The extract using methanol:water solvent showed the phytochemical content of triterpenoids, flavonoids, saponins and tannins (Saha et al., 2013). The ethanol

extract and ethyl acetate fraction contain flavonoids, phenolics and terpenoids (Anam et al., 2023). The results of this study show that most of the secondary metabolite compounds in *Centella asiatica* leaves are polar and semi-polar, while the n-hexane solvent is a non-polar solvent. Polar compounds will dissolve in polar solvents and non-polar compounds will dissolve in non-polar solvents (Lindawati & Ma'ruf, 2020).

Table 2. Total Phenolic Content of *Centella asiatica* Leaves

Sample	Total Phenolics (mg GAE/g)
Ethanol Extract 70%	12.773 ± 0.479^{c}
n-Hexane Fraction	1.182 ± 0.124^{a}
Ethyl Acetate Fraction	18.334 ± 0.305^{d}
Methanol:Water Fraction	10.211 ± 0.247^{b}

Note: Numbers followed by different letters indicate differences significant in Tukey test ($p < 0.05$)
Measuring instrument: UV-Vis Spectrophotometer

Phenolic content is an active compound that has garnered significant attention due to its potential and the beneficial effects it offers to human health. Phytochemical screening of extracts and fractions of *Centella asiatica* leaves showed the presence of phenolic compounds. Therefore, a quantitative test was carried out for the total phenolic content using the Folin-Ciocalteu reagent and the results are presented in Table 2. Ethyl acetate solvent showed the highest total phenolic content 18.334 ± 0.305 mg GAE/g extract, followed by ethanol solvent 12.773 ± 0.479 mg GAE/ g extract and methanol:water solvent 10.211 ± 0.247 mg GAE/g extract. This shows that most phenolic compounds are extracted with ethyl acetate solvent. According to previous research, ethyl acetate solvent is a semipolar solvent that is capable of filtering phenolic compounds and is more effective than water, ethanol and n-hexane (Sulistyarini et al., 2022). The results of analysis using ANOVA showed that ($p < 0.05$) treatment with extraction and fractionation methods and with different solvents produced different total phenolic contents.

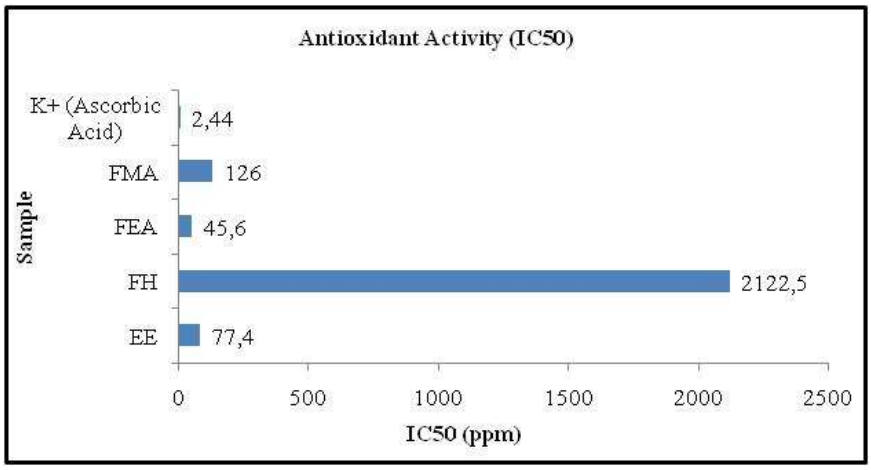

Figure 2. Antioxidant Activity (IC_{50}) of *Centella asiatica* Leaves
Measuring instrument: UV-Vis Spectrophotometer

The results of the antioxidant activity test (Figure 2) showed that the ethyl acetate fractions FEA provided a very strong inhibitor against DPPH free radicals with the smallest IC_{50} value of 45.6 ppm, followed by ethanol extract (EE) with a value of 77.4 ppm, fraction methanol:water (FMA) with a value of 126 ppm and n-hexane fraction (FH) with a value of 2122.5 ppm. Antioxidant activity with different solvents showed significantly different IC_{50} values ($p < 0.05$). Antioxidant activity is closely related to the total phenolic content in the sample. Previous studies regarding the effect of salinity on the growth of *Centella asiatica*

showed a very strong correlation between total phenolics and antioxidant activity (Hoang & Rehman, 2022). In general, compounds that have antioxidant activity are phenol compounds, this is due to the presence of hydroxy groups distributed on the benzene ring in the ortho and para positions to the –OH and –OR groups. The hydroxyl group acts as an electron donor against free radicals (Irianti et al, 2021).

The ethyl acetate fraction (FEA) showed the highest total phenolic content of 18.334 ± 0.305 mg GAE/g (Table 2) with an IC_{50} value of 45.6 ppm (Figure 2) indicating a very strong antioxidant because the IC_{50} value was < 50 ppm (Indraningrat et al., 2023). The second highest total phenolic content with ethanol solvent was 12.773 ± 0.479 mg GAE/g (Table 2) with an IC_{50} value of 77.4 ppm (Figure 2) indicating strong antioxidant activity because the IC_{50} value was 50-100 ppm (Indraningrat et al, 2023). According to (Anam et al., 2023), the highest antioxidant activity was identified in the ethyl acetate fraction of *Centella asiatica* (EAF) of 102.57 ± 3.40 ppm, compared to the ethanol extract of 300.88 ± 43.78 ppm and the ethanol fraction of 494.96 ± 25.10 ppm. This is because EAF contains many phenolic compounds and contains flavones 5,7,2',5'- Tetrahydroxy-flavones which are free aglycone flavonoids which are thought to have antioxidant activity. However, this compound is not contained in the ethanol fraction (EF) of *Centella asiatica* because it cannot dissolve in polar solvents due to its chemical structure (Anam et al. 2023).

The antioxidant activity of *Centella asiatica* leaf extract was compared with that of ascorbic acid (K+). The results show that the solvent ethyl acetate when compared with ascorbic acid (Figure 2) both have very strong antioxidant capabilities because the IC_{50} value is <50 ppm (Indraningrat et al. 2023). Ascorbic acid is white crystals that are soluble in water but are easily damaged by contact with air. Ascorbic acid is an antioxidant agent that can reduce free radicals, protect DNA, amino acids and lipids from oxidation (Cimmino et al., 2018). Ascorbic acid acts as a donor of hydrogen atoms, reacts with superoxide radicals, hydrogen peroxide forms monodehydroascorbic acid which can be reducted back into ascorbic acid so that free radicals can be neutralized and become no longer reactive (Basuki, 2019).

Phenolic compounds consist of many hydroxyl groups which can become proton donors to stabilize DPPH. Phenolic compounds are the most abundant secondary metabolites in plants which have an important effect in eliminating excessive ROS (*Reactive Oxygen Species*). Flavonoids are a group of phenolic compounds and are known to have antioxidant properties (Hasanuzzaman et al., 2021). Phenolic compounds support the immune system, have antibacterial, antiviral and antifungal properties and protect the skin against UV radiation (Tungmunnithum et al., 2018). The ability of phenolic compounds as antioxidants is due to the presence of a hydroxyl group attached to the aromatic ring in phenolic compounds, causing these compounds to be easily oxidized by donating hydrogen atoms to free radicals. This causes phenolic compounds to change into phenoxyl radicals in the oxidation reaction, giving phenolic compounds the potential to act as antioxidants (Rohmanna et al., 2023).

CONCLUSION

The results showed that the 70% ethanol extract, ethyl acetate fraction and methanol:water fraction of *Centella asiatica* leaf have the potential as natural antioxidants and are effective in extracting phytochemical components. Ethyl acetate solvent has the highest total phenolic content, namely 18.334 ± 0.305 mg GAE/g with the smallest IC_{50} value of 45.6 ppm, which shows very strong antioxidant activity.

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