MEDFARM: Jurnal Farmasi dan Kesehatan, Vol. 14, No. 2, 2025, Page 527-539
e-ISSN : 2715-9957
p-ISSN: 2354-8487

Antidiarrhoeal Potential of Secondary Metabolites in Betel Leaf (Piper betle): A Systematic Review with Radar Chart Analysis and AUC Evaluation.

Khrisna Agung Cendekiawan[1,2], Kintoko [1*], Sapto Yuliani [1], Linda Suci Anggraeni[2] Firdha Aprillia Wardhani[3], Neny Poerwahyuningrum[3]

[1)]Departement of Doctoral Pharmacy, Faculty of Pharmacy, University of Ahmad Dahlan, Jogjakarta
[2)]Departement of Bachelor Pharmacy, Faculty of Health Sciences, University of dr. Soebandi, Jember
[3)]Faculty of Pharmacy, University of Jember

e-mail:
kintoko@pharm.uad.ac.id)

ABSTRACT

Diarrhoea is a widespread gastrointestinal disorder commonly caused by microbial infection, inflammation, or impaired intestinal function. While synthetic antidiarrhoeal drugs are available, their use is often limited by adverse effects and antimicrobial resistance, prompting increasing interest in medicinal plants such as *Piper betle* (betel leaf). This study systematically reviewed the literature to identify secondary metabolite compounds in *Piper betle* with antidiarrhoeal potential and to evaluate their biological activities using Radar Chart Analysis (RCA) and Area Under Curve (AUC) methods. A systematic search was performed across PubMed, Scopus, Web of Science, and Google Scholar using predefined keywords. Inclusion criteria comprised studies that investigated *Piper betle* or its secondary metabolites, reported antidiarrhoeal or related bioactivity, and provided quantitative data suitable for comparison. Studies were excluded if they focused solely on synthetic drugs, were not available in full text, or did not report measurable metabolite data. A total of 35 eligible studies were included after screening 176 records. The findings indicate that flavonoids, polyphenols, tannins, saponins, and catechins in *Piper betle* contribute to antidiarrhoeal effects through mechanisms that modulate intestinal motility, reduce fluid secretion, activate anti-inflammatory pathways, and exhibit antimicrobial activity. RCA and AUC analyses further demonstrated substantial variability in metabolite composition and antioxidant capacity across studies. Overall, *Piper betle* exhibits promising therapeutic potential as a natural antidiarrhoeal agent, although further mechanistic and clinical research is warranted.

Keywords: *Medicinal plants, secondary metabolites, antidiarrhoeal, mechanism*.

Introduction

Indonesia is recognized as one of the world's megabiodiversity countries, possessing extensive tropical forests and a rich variety of medicinal plants. More than 30,000 plant species have been identified across the archipelago, and approximately 1,000 species are documented as having medicinal potential, with at least 300 species traditionally utilized by local communities for health-related purposes (Ministry of

Environment and Forestry, 2020; Rahayu et al., 2019). The use of traditional medicine continues to increase not only in developing countries but also in developed nations. The World Health Organization (WHO) reports that up to 80% of the population in developing countries relies on traditional medicine for primary healthcare. In comparison, its use in developed countries reaches approximately 60% due to growing concerns about the adverse effects of synthetic drugs and the global trend toward natural therapies (WHO, 2014; Ekor, 2014).

Ethnomedicine, a field that examines traditional healing knowledge and cultural health practices, plays a significant role in the discovery of new therapeutic agents. As a discipline rooted in indigenous knowledge systems, ethnomedicine offers insights into plant-based treatments that have been safely used for generations. Research in this area is essential for identifying novel bioactive compounds, addressing the limitations of existing drugs, and overcoming challenges such as antimicrobial resistance and emerging diseases (Heinrich et al., 2020; Jamshidi et al., 2018).

Diarrhoea remains one of the most common gastrointestinal disorders worldwide, associated with high morbidity and mortality, particularly in low- and middle-income countries. It can result from microbial infections, inflammatory bowel conditions, food intolerances, and adverse reactions to medications (WHO, 2023). Conventional antidiarrhoeal drugs, such as loperamide and antibiotics, may provide clinical benefits but are often limited by side effects, increasing antimicrobial resistance, and poor patient tolerability (Thapar & Sanderson, 2004; Shane et al., 2017). These limitations have driven global interest in medicinal plants as alternative or complementary antidiarrhoeal therapies.

One of the medicinal plants widely used in Southeast Asia is betel (Piper betle L.), a species belonging to the Piperaceae family. Betel leaves have been traditionally utilized for antiseptic, anti-inflammatory, antibacterial, antifungal, antihelminthic, carminative, and wound-healing purposes (Prakash et al., 2010). Phytochemical investigations reveal that *Piper betle* contains abundant secondary metabolites, including flavonoids, tannins, alkaloids, polyphenols, and saponins, which contribute to diverse pharmacological activities (Guha, 2006; Arambewela et al., 2005). Several of these compounds have been associated with antidiarrheal mechanisms, including the inhibition of intestinal motility, reduction of intestinal secretion, modulation of gut microbiota, and anti-inflammatory effects (Hossen et al., 2020; Prajapati et al., 2017).

Despite the increasing evidence regarding the therapeutic potential of *Piper betle*, specific mechanisms underlying the antidiarrhoeal activity of its secondary metabolites remain insufficiently understood. Furthermore, comparative interpretation of metabolite levels—such as polyphenols, flavonoids, and catechins—requires structured quantitative visualization. Radar Chart Analysis (RCA) and Area Under Curve (AUC) calculations provide robust approaches for evaluating multivariate parameters and understanding the proportional contribution of each metabolite to biological activity (Sahu et al., 2018).

Therefore, this systematic literature review aims to (1) identify secondary metabolite compounds present in *Piper betle* with potential antidiarrhoeal activity,

(2) explore the biological mechanisms involved, and (3) analyze quantitative parameter patterns using Radar Chart Analysis (RCA) and Area Under Curve (AUC) methods. This review is expected to provide comprehensive insights into the medicinal potential of betel leaves and support future pharmacological research.

Methodology

Search Strategy

A systematic search was conducted across four major databases—PubMed, Scopus, Web of Science, and Google Scholar—to identify relevant studies on secondary metabolites of *Piper betle* and their antidiarrhoeal activity. The search generated a total of 176 records. After removing duplicates, 150 articles remained for the screening phase. Titles and abstracts were screened based on predefined inclusion criteria, which required studies to investigate *Piper betle* or its secondary metabolites, report antidiarrhoeal or related biological activities, and provide quantitative data suitable for further analysis. During this stage, 50 articles were excluded because they were irrelevant to the study's focus.

The remaining 100 articles were assessed for full-text eligibility. Full-text evaluation considered the availability of complete data, relevance to antidiarrhoeal mechanisms, and clarity of experimental results, as well as the presence of measurable parameters relevant to Radar Chart Analysis (RCA) and Area Under Curve (AUC) calculations. A total of 65 full-text articles were excluded for reasons such as insufficient data, lack of quantitative metabolite information, non-inclusion of *Piper betle*, or exclusive focus on synthetic drugs.

Ultimately, 35 studies met all eligibility criteria and were included in the final qualitative synthesis. These studies formed the basis for discussions of secondary metabolite profiles, antidiarrheal mechanisms, and subsequent RCA and AUC analyses. The complete selection process follows the PRISMA framework and is presented through the identification, screening, eligibility, and inclusion stages. Articles published between 2000 and 2024 were included in this review.

Inclusion and Exclusion Criteria

Articles selected for this review have to meet the inclusion criteria:

- Studies that identified polyphenol, flavonoid and catechin secondary metabolite compounds in Betel with antidiarrhoeal effects.
- Studies that reveal the mechanism of antidiarrhoeal action and antioxidant inhibition of these compounds.
- Experimental studies (in vitro, in vivo) or relevant clinical trials.

  As for the exclusion criteria, publications of studies that evaluate the antidiarrhoeal effect with synthetic drugs, or studies that do not involve secondary metabolite compounds in medicinal plants, are excluded.

Selection Procedure

Articles found from the initial search were screened based on keywords, title and abstract. Articles that met the inclusion criteria were then further analyzed by reading the full text. Data obtained from eligible articles were qualitatively analyzed to identify secondary metabolite compounds and the mechanisms of action involved.

Result and Discussion

Percent Level of Polyphenols in Betel Leaf

Polyphenols are a group of chemicals found in plants and exist in the form of polar glycosides and are readily soluble in polar solvents (Hosttetman, et al, 1985). Some classes of essential polymeric materials in plants, such as lignin, melanin, and tannin, are polyphenolic compounds, and sometimes phenolic units are found in proteins, alkaloids, and terpenoids (Harbone, 1987). All phenol compounds are aromatic compounds so they all show strong absorption in the UV region of the spectrum. In addition, phenol compounds characteristically show a bathochromic shift in their spectra when bases are added. Therefore, the method of spectrometry is important, especially for the identification and quantitative analysis of phenol compounds (Harbone, 1987).

In the literature review on the topic of the percentage of polyphenol content in betel leaf, in Table 1, the average research uses betel leaf extract to determine the polyphenol content in betel leaf extract. According to several research results, there are variations in polyphenol content in betel leaf extracts. In the research by Candra Irawan et al. in 2024, the content was 758,534 ± 0.003 mg GAE per gram of sample. The extraction method used was Ultrasound-Assisted Extraction (UAE) at room temperature for 30 minutes, resulting in 8.47% extract. Followed by research in the same year, by Abdullah et al in 2024, stated that there was a polyphenol content of 25.68 ± 0.29 mg GAE/g extract which has potential as an antioxidant and antibacterial activity.

Table 1. Betel Leaf Research with Parameters % polyphenol content (Poudel et al., 2024)

Sample Name	Parameters % polyphenol content
Piper Leaf	https://doi.org/10.52711/0974-360X.2024.00176 showed that the total phenolic content in black species of betel leaf extract (*Piper betle L. various Nigra*) was **758,534 ± 0.003 mg** GAE per gram sample. The extraction method used was Ultrasound-Assisted Extraction (UAE) at room temperature for 30 minutes, yielding 8.47% extract. This high phenolic content suggests potential health benefits, especially in antioxidant and anti-gout applications. The highest TPC level of 13 total phenol content obtained by guava leaf extract was 190 g/100 g per cup.
	The journal "Estimation of Phytochemical Constituents and Evaluation of Antioxidant Potency of *Piper betle* Leaves", showed that the total phenolic content (TPC) in betel leaves (*Piper betle*) was quantified at **51.5278 mg GAE/gm**. This indicates the presence of significant polyphenols, which are known for their antioxidant properties (Poudel et al., 2024).
	https://doi.org/10.30997/ijar.v5i2.486 showed that the TPC in the n-hexane extract of red betel leaves (*Piper crocatum*) was found to be **25.68 ± 0.29 mg**

GAE/g. This indicates the presence of significant polyphenols in the extract, which contribute to its biological activity (Abdullah et al., 2024).

https://doi.org/10.31276/VJST.64(3).37-42 showed that the total phenolic content in betel leaf extract obtained using 96% ethanol was measured at **386.34 mg GAE/g extract** (Hoang et al., 2022).

The journal "Biochemical analysis of betel vine (*Piper betle*) leaves", showed that the total phenolic content in betel leaves (*Piper betle*) was found to range from **94.98 to 95.18 mg per 100g**. This indicates the presence of a significant content of polyphenols, which are known for their antioxidant properties (Kubade et al., 2021).

Percent Flavonoid Content In Betel Leaf

The use of flavonoids in plants is to provide maintenance against stress conditions by the environment, regulate plant growth, maintenance from ultraviolet radiation rays and attraction to insect pollinators, fungi, viruses, and bacteria (Vidak, 2015). Apart from being hormone controllers and enzyme inhibitors, flavonoids also play a role in UV filtration, symbiotic fixation and flower pigmentation (Gupta, 2015). While in humans, flavonoids act as stimulants to the heart, diuretics, stabilize blood sugar levels, antifungal, anti-inflammatory, antitumor, antiallergic, antibacterial, and can prevent osteoporosis (Salmia, 2016). In the literature review on the topic of the percentage of flavonoid content in betel leaf, Table 2 presents the average research that uses betel leaf extract to determine the flavonoid content. According to some of the research results, there were variations in flavonoid content in betel leaf extracts. In the research of Melina Poudel et al in 2024, there was a content of 33.769 mg of total flavonoids GAE/g DW which has benefits as an antioxidant.

Table 2. Betel Leaf Research with Parameters % flavonoid content (Nursamsiar et al.,2023)

Sample Name	Parameter % flavonoid content
Piper Leaf	In the journal "Extraction of Flavonoid Compounds from Red Betel Leaves (*Piper Crocatum*) Using Ultrasound-Assisted Extraction (UAE) Method", showed that the highest flavonoid content obtained from red betel leaves (*Piper crocatum*) using the Ultrasound-Assisted Extraction (UAE) method was **263.676 mgQE/g**.
	The journal "Estimation of Phytochemical Constituents and Evaluation of Antioxidant Potency of *Piper betle* Leaves", showed that the total phenolic

content (TPC) in betel leaves (*Piper betle*) was quantified at **51.5278 mg GAE/gm**. This indicates the presence of significant polyphenols, which are known for their antioxidant properties (Poudel et al., 2024).

http://www.doi.org/10.26538/tjnpr/v7i8.7 showed that the total flavonoid content in red betel leaves was measured as follows: sonication method yielded **11.4 ± 0.31 mgEQ/g**, reflux method yielded **16.1 ± 0.42 mgEQ/g**, and Soxhlet method yielded **11.8 ± 0.05 mgEQ/g**. For green betel leaf, sonication method yielded **10.9 ± 0.11 mgEQ/g**, reflux method yielded **6.4 ± 0.14 mgEQ/g**, and Soxhlet method yielded **17.6 ± 0.09 mgEQ/g** (Nursamsiar et al., 2023).

https://doi.org/10.32585/bjas.v2i2.936 shows that the flavonoid content in green betel leaves (*Piper betel linn*) increases up to 0.09% after drying in the oven for 8 hours at 40°C, after the initial drying method without an oven. Oven drying increased the flavonoid content compared to sun drying alone (Setyabudi et al., 2020).

Percent Catechin Content In Betel Leaf

Catechins are secondary metabolite compounds naturally produced by plants and belong to the flavonoid class. This compound has antioxidant properties thanks to its phenol group. This component in the body can act to repair cognitive damage, inhibit the process of fat accumulation and many other benefits. Catechins also have important biological compound activities such as anti-tumor and anti-oxidant activities. Flafon-3-ol epicatechin and catechin (Putri, 2010). In addition, medically, catechin compounds in tea have many benefits such as being able to reduce the risk of cancer, tumors, lower cholesterol, prevent hypertension, kill bacteria and fungi, and kill influenza viruses (Alamsyah, 2006). Polyphenols also strengthen the defense mechanism of an organism, have anti-microbial, anti-cancer, and antioxidant properties (Otarini, 2009).

In the literature review with the topic of the percentage of catechin content in betel leaves on table 3, the average research uses betel leaf extract to determine the catechin content in betel leaf extract. From several research results, variations in catechin content in betel leaf extract were found. In the research of Xiaoyan Shen et al in 2024, there was the highest catechin content and showed the most effective transformation of catechins into theaflavin (TF) and thearubigin type SII (SII-TR) during suspended fermentation, achieving a TF conversion ratio of 13.96% and a SII-TR conversion ratio of 13.02% after 120 minutes. This research then became the basis in the analysis of catechins that can undergo biotransformation into other compounds to be analyzed for their properties.

Table 3. Betel Leaf Research with Parameters of % Catechin Content (Shen et al., 2024)

Sample Name	Parameter % catechin content
Piper Leaf	In the journal "Estimation of Phytochemical Constituents and Evaluation of Antioxidant Potency of Piper betle Leaves", shows that The total phenolic content (TPC) was measured at **51.5278 mg GAE/gm**, and the total flavonoid content (TFC) was recorded at **33.769 mg QE/gm**, indicating a strong potential for these leaves to act as natural antioxidants (Poudel et al., 2024).
	The journal "Advances in Biosynthesis Pathways and Regulation of Flavonoids and Catechins", points out that this study highlights the importance of flavonoids, particularly catechins, in tea plants, noting that flavonoids constitute **12%-25%** (Tao & Gao, 2009).
	In the journal "Isolation and Quantitative Analysis of a Bioactive Polyphenol -Catechin in Anacardium occidentale Linn. (Leaves and Testa) by HPLC Analysis", showed that the Catechin was found to be **99.30%** based on the comparison of peak purity and peak area of isolated Catechin and Catechin markers. (Jaiswal, 2010).
	https://doi.org/10.1017/S0007114519003131 showed that (+)-catechin and (-)-epicatechin concentrations in **24%** urine samples were analyzed using tandem mass spectrometry after enzymatic deconjugation(Aguilera et al., 2021).
	https://doi.org/10.1016/j.jfca.2024.106596 showed that the tea variety Xiaoxianghong 21-3 (XXH21-3) exhibited the highest catechin content and showed the most effective transformation of catechins into theaflavin (TF) and thearubigin type SII (SII-TR) during suspended fermentation, achieving a TF conversion ratio of **13.96%** and a SII-TR conversion ratio of **13.02%** after 120 minutes (Shen et al., 2024).

Percent Inhibition of Antioxidants In Betel Leaf

Antioxidants are substances that have the potential to capture free radicals and highly reactive molecules, thereby inhibiting oxidation reactions that can initiate damage to the human body. The process of inhibiting antioxidant reactions can potentially increase the likelihood of damage to human body parts, so it is necessary to research the potential of antioxidants.

In the literature review on the topic of the percentage of inhibition of antioxidant activity in Betel leaf samples, Table 4 presents the average research that uses Betel leaf extract to determine the extent of its potential in inhibiting antioxidant activity. According to some of the research results, there were variations in the potential antioxidant activity inhibition in betel leaf extracts. In the research by Naida Almira et al. in 2023, antioxidant inhibition potential was observed at several concentrations. The results showed that at concentrations of 2 ppm, 4 ppm, 6 ppm, 8 ppm, and 10 ppm were measured, showing an inhibition of 54%. Then, in the research of Weni et al in 2023, testing was conducted at a concentration of 200 ppm, showing inhibition of fatty acid oxidation by 52.13%, which indicates its antioxidant activity. This study found no significant difference in the inhibition of unsaturated fatty acid oxidation between red betel extract and α-tocopherol at the same concentration.

Table 4. Research of Betel Leaf with Parameters of % antioxidant inhibition (Nursamsiar et al., 2023)

Sample Name	Parameter % antioxidant inhibition
Daun Sirih	https://doi.org/10.30997/ijar.v4i3.374 showed that red betel leaf extract (*Piper crocatum*) at a concentration of 200 ppm showed inhibition of fatty acid oxidation by 52.13%, indicating its antioxidant activity. (Weni & Safithri, 2023).
	https://doi.org/10.37874/ms.v8i3.823 shows that the percentage of inhibition of ethanol extract of Chinese betel leaves (ECBL) showing an inhibition of **54%** (Almira et al., 2023).
	https://doi.org/10.33859/jpcs.v4i1.422 shows that the percentage of antioxidant inhibition in red betel leaves (Piper crocatum) was found to be **81.82%** at an extract concentration of 80 ppm (Tonahi et al., 2014).
	https://doi.org/10.22376/ijpbs.2016.7.4.p323-328 showed that the half-maximal inhibitory concentration (IC50) of the methanolic extract of Piper betel leaves was found to be **56.88 µg/ml**, indicating its effective antioxidant properties. (Muthukumarasamy & Ain Najihah Mohd Ideris, 2016)
	The journal "Free Radicals Scavenger Potency of Betel Leaves (*Piper betle* L.) Extract and Various Fractions", showed that this study did not provide a specific percentage of antioxidant inhibition in betel leaves. However, this study showed that betel leaf extract and its fractions exhibited significant free radical with the highest DPPH found in gallic acid (**IC50 0.732 µg/mL**) and butanol fraction showing the highest H2O2 (**IC50 0.223 µg/mL**) (Widowati et al., 2010).

Percent Antidiarrhoeal Potential In Betel Leaf

Diarrhoea is a common condition experienced by many people. Although it is often considered a minor nuisance, diarrhoea can be a sign of a more serious health problem that requires medical attention. Diarrhoea is defined as a condition where a person experiences an increased frequency of bowel movements with liquid or watery stools. It can be accompanied by other symptoms such as nausea, vomiting, abdominal cramps, and sometimes weight loss. The potential of Betel leaf as an antidiarrhoeal can be utilized by the community as a useful medicinal plant.

In the literature review on the topic of the percentage of antidiarrhoeal activity in Betel leaf samples in Table 5, the average research uses Betel leaf extract to determine the potential of Betel leaf extract in overcoming diarrhoea. According to some research results, variations in the potential antidiarrheal activity of betel leaf extract were observed. In the research of Vishal Tarmale et al in 2024, it was found that the potential antioxidant activity reached 30%. As for the weight of the extract that can be used from Betel leaf samples of 150-300mg/Kg, based on research from Nurhalimah et al in 2015.

Table 5. Betel Leaf Research with Parameters of % antidiarrhoeal potency (Poudel et al., 2024)

Sample Name	Parameter % antidiarrhoeal potential
	The study https://doi.org/10.14710/jksa.26.6.224-229 demonstrated that the essential oil extracted from green betel leaves exhibited significant antibacterial activity, specifically against Staphylococcus epidermidis and Escherichia coli, with optimal inhibition observed at concentrations of **75% and 90%**, respectively. Chemical analysis via GC-MS identified 44 components in the essential oil, with acetyl cavicol, germacrene-D, and eugenol being the most abundant. (Fachriyah et al., 2023).
Piper Leaf	In the journal "Antidiarrhoeal Effects of Beluntas Leaf Extract (*Pluchea indica* L.) Against Male Mice Induced By Bacteria Salmonella Typhimurium Antidiarrhoeal Effects Beluntas Leaf Extract (*Pluchea indica* L.) Against Male Mice Induced By Bacteria Salmonella Typhimurium", shows that beluntas leaf extract (*Pluchea indica* L.) has antidiarrhoeal effects on male mice induced by Salmonella typhimurium, showing significant antidiarrhoeal effects in male mice induced by Salmonella typhimurium, particularly at doses of **150 mg/kg and 300 mg/kg**, which gave results comparable to the standard antidiarrhoeal drug loperamide. (Nurhalimah et al., 2015).
	https://doi.org/10.69613/hanf0a52 points out that this paper presents specific quantitative data regarding the percentage of antidiarrheal activity in betel leaf (Piper betle L.) at **30%**. However, the paper highlights the traditional use of betel leaf for a variety of therapeutic purposes, including indigestion (Tarmale et al., 2024).

https://10.1007/s11655-013-1334-1 shows that the phytochemical composition of betel leaf has been analyzed through various extraction methods, including the use of ethanol and chloroform extracts, which have demonstrated significant biological activities of **41%** such as antimicrobial, antifungal, and anticariogenic effects.

https://doi.org/10.1515/jbcpp-2015-0165 indicates that This study evaluated the antidiarrhoeal effects of **15%** of the ethanol extract and its fractions by performing tests such as castor oil-induced diarrhoea, castor oil-induced enteropooling, and gastrointestinal transit tests in mice (Akhter et al., 2023).

Determination of Area Under Curve value and Radar Chart Analysis

AUC stands for Area Under the Curve, which is a measure of the part of the curve that shows the drug concentration required for a person to achieve optimal therapeutic effects. The use of AUC in specific calculation formulas is crucial to ensure that patients receive the optimal dose of drugs that work and minimize the occurrence of side effects (toxicity) caused by certain medications, especially those affecting the kidneys. If the AUC is too high, the risk of toxicity increases, and if it is too low, the drug will not work effectively. Therefore, AUC is currently a recommendation for one part that needs to be seen in the use of drugs, so that the drug works optimally and provides minimal toxicity to the body.

Table 6. Calculation of Average Value of each Parameter (2025)

	Parameters				
Sample Name	% polyphenol content	% flavonoid content	% catecin content	% antioxidant inhibition	% antidiarrhoeal activity
Piper Leaf	75,534	26,676	25	52.13	75
	51,278	55,278	12	54	90
	25,68	33,769	13,65	81.82	30
	38,634	11,4	24	56.88	41
	95,18	49	13,96	26.01	15
Mean	**33,089**	**23,154**	**37**	**270.84**	**50.2**

Based on the data table 6 obtained, calculations for Radar Chart Analysis (RCA) and AUC can be performed. RCA is a graphical method for displaying multivariate data in a two-dimensional graph of more than two quantitative variables represented by axes starting from the same point. RCA is a graph and/or plot consisting of radii that describe the value of one variable. The length of the radius is equal to the magnitude of the

MEDFARM: Jurnal Farmasi dan Kesehatan, Vol. 14, No. 2, 2025, Page 527-539
e-ISSN : 2715-9957
p-ISSN: 2354-8487

variable value. then a line is drawn connecting the data values. This forms a radar or star-shaped plot in Figure 1.

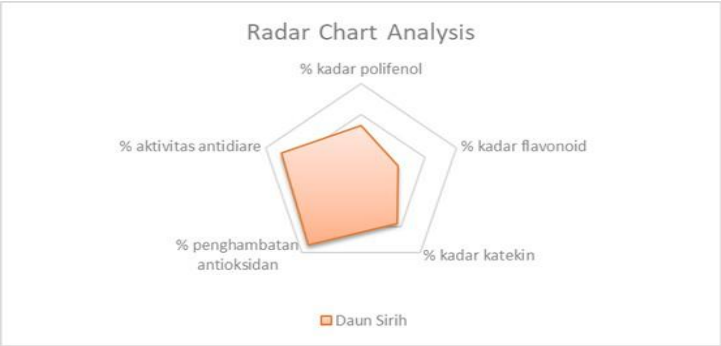

Figure 1. Radar Chart Analysis of Betel Leaf (2025)

The AUC calculation uses the trapezoidal formula based on the average value of each parameter. From the calculation results in Table 7, a graph of each parameter will be obtained.

Table 7. AUC calculation (2025)

X	Y	Calculation	AUC
0	0	0	0
1	33.09	((0+33.09)/2)*(1-0)	16.545
2	23.15	((33.09+23.15)/2)*(2-1)	28.12
3	37.00	((37.00+23.15)/2)*(3-2)	30.075
4	54.00	((54.00+37.00)/2)*(4-3)	45.5
5	50.20	((50.20+54.00)/2)*(5-4)	52.1
TOTAL			172.34

As shown in Figure 2, the AUC was determined by applying the trapezoidal formula to the graph. The individual AUC calculations were then combined to arrive at the total AUC value.

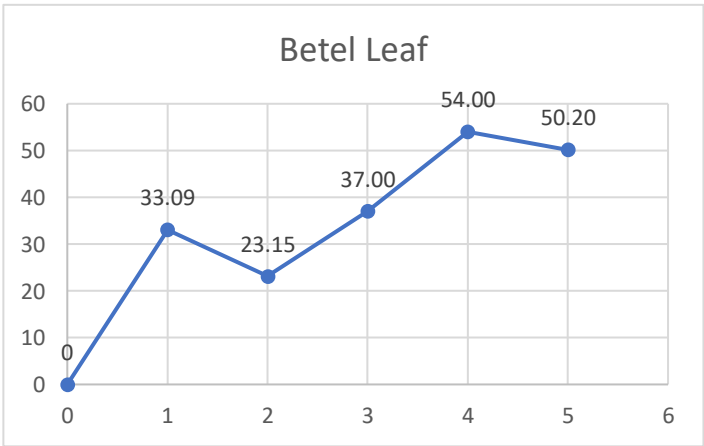

Figure 2. Betel Leaf Parameter Chart (2025)

Conclusion

This study showed that secondary metabolites in betel leaf, such as flavonoids, polyphenols, and catechins, have potential antidiarrheal effects through biological mechanisms and antioxidant activity. Although the existing research is promising, more studies are needed to fully understand the molecular mechanisms and therapeutic potential of medicinal plants in treating diarrhea.

Declaration of Competing Interest

The authors declare that they have no competing interests

Reference

Abdullah, W., Seno, D. S. H., & Safithri, M. (2024). Total Phenolics, Flavonoids, and α-Glucosidase Inhibitory Activity of Red Betel (Piper crocatum) Extract in Various Solvents. *Indonesian Journal of Applied Research (IJAR)*, *5*(2), 112–123. https://doi.org/10.30997/ijar.v5i2.486

Akhter, N., Alam, M., Amin Khan, M. R., Sharmin, S., Emon, N. U., Bakar Siddique, M. A., Hossain, K. H., & Rahman, M. A. (2023). Therapeutic potentials of Adenostemma lavenia (L.) O.Kuntze evidenced into an array of pharmacological effects and ligand-receptor interactions. *Heliyon*, *9*(4). https://doi.org/10.1016/j.heliyon.2023.e15541

Almanza-Aguilera, E., Ceballos-Sánchez, D., Achaintre, D., Rothwell, J. A., Laouali, N., Severi, G., Katzke, V., Johnson, T., Schulze, M. B., Palli, D., Gargano, G., de Magistris, M. S., Tumino, R., Sacerdote, C., Scalbert, A., & Zamora-Ros, R. (2021). Urinary concentrations of (+)-catechin and (-)-epicatechin as biomarkers of dietary intake of flavan-3-ols in the european prospective investigation into cancer and nutrition (epic) study. *Nutrients*, *13*(11). https://doi.org/10.3390/nu13114157

Fachriyah, E., Fadillah, H., Sarjono, P. R., & Ismiyarto, I. (2023). Isolation, Identification, and Antibacterial Testing of Essential Oil from Green Betel Leaf (Piper Betle L.) Using Well Diffusion Method. *Jurnal Kimia Sains Dan Aplikasi*, *26*(6), 224–229. https://doi.org/10.14710/jksa.26.6.224-229

Hoang, T. D., Nguyen, K. T. K., Ngo, H. L., Phan, T. K. N., Lam, H. A. T., Pham, T. D., Ngo, V. K. T., & Nguyen, H. T. (2022). Evaluation of bioactivities of ultrasound-assisted extraction of betel leaves (Piper betle L.). *Ministry of Science and Technology, Vietnam*, *64*(3), 37–42. https://doi.org/10.31276/VJST.64(3).37-42

Jeane Maria Mustika Tonahi, Siti Nuryanti dan Suherman. (2014). Antioksidan Dari Daun Sirih Merah (*Piper crocatum*). Jurnal Akademi Kimia. 3(3): 158-164.

Kubade, K., Phule Krishi Vidyapeeth, M., Jaybhay Mahatma Phule Krishi Vidyapeeth, I. V., Patil, B., Jaybhay, V., Shewale, S., & Nakhate, P. (2021). Biochemical analysis of betel vine (Piper betel) leaves. *~ 353 ~ The Pharma Innovation Journal*, *10*(1), 353–355. http://www.thepharmajournal.com

Muthukumarasamy, R., & Ain Najihah Mohd Ideris, N. (2016). Formulation And Evaluation of Antioxidant Cream Containing Methanolic Extract Of Piper Betel Leaves. *Int J Pharm Bio Sci*, *7*(4), 323–328. www.ijpbs.net

Nurhalimah, H., Wijayanti, N., & Widyaningsih, T. D. (2015). Efek Antidiare Ekstrak Daun Beluntas pada Mencit-Nurhalimah, dkk. In *Jurnal Pangan dan Agroindustri* (Vol. 3).

Nursamsiar, N., Marwati, M., & Nur, S. (2023). The Effect of Extraction Method on Flavonoid Content and Antioxidant Activity of Red Betel and Green Betel Extracts. *Tropical Journal of Natural Product Research*, *7*(8), 3620–3625. https://doi.org/10.26538/tjnpr/v7i8.7

Poudel, M., Koirala, N., Mehta, R. K., & Lamsal, A. (2024). Estimation of Phytochemical Constituents and Evaluation of Antioxidant Potency of Piper betle Leaves. *Nepal Journal of Biotechnology*, *12*(1). https://doi.org/10.54796/njb.v12i1.300

Rahma Almira, N., Ahidin, D., & Indawati, I. (2023). PHYTOCHEMICALS SCREENING AND ANTIOXIDANT ACTIVITY TEST OF ETHANOLIC EXTRACT OF CHINESE BETEL LEAVES (Peperomia pellucida L.) AND ITS FRACTIONS. In *Medical Sains : Jurnal Ilmiah Kefarmasian* (Vol. 8, Issue 3).

Setyabudi, S., Yakin, E. A., & Sukaryani, S. (2020). Analysis of Tannin and Flavonoid Contents of Green Sirih Leaves (Piper betel linn) of Green Different in Physical Conditions. In *Bantara Journal of Animal Science p* (Vol. 2, Issue 2).

Tao, X., & Gao, L.-P. (2009). Advances in Biosynthesis Pathways and Regulation of Flavonoids and Catechins. *Scientia Agricultura Sinica*, *42*(8), 2899–2908. https://doi.org/10.3864/j.issn.0578-1752.2009.08.031

Vishal Ananta Tarmale, Sachin Wankhede, Abhishek Kumar Sen, & Sonali Vinod Uppalwar. (2024). Pharmacological Properties, and Traditional Applications of Betel Leaf (Piper betle L.). *Journal of Pharma Insights and Research*, *2*(6), 131–141. https://doi.org/10.69613/hanf0a52

Weni, M., & Safithri, M. (2023). Antioxidant Activity and Tyrosinase Inhibitor of Red Betel Leaf Extract. *Indonesian Journal of Applied Research (IJAR)*, *4*(3), 234–245. https://doi.org/10.30997/ijar.v4i3.374

Widowati, W., Wargasetia, T. L., Khiong, K., Mozef, T., Soeng, S., & Risdian, C. (2010). Free Radicals Scavenger Potency of Betel Leaves (Piper betel L.) Extract and Various Fractions Potensi Pemerangkapan Radikal Bebas Ekstrak dan Fraksi-fraksi Daun Sirih (Piper betel L.). In *JKM* (Vol. 10, Issue 1).

Xiaoyan Shen, Xiaofen Wu, Hui Qi, Du Wen, Ming Deng, Keqin Wang, An Liu, Liang Chen (2024). *Oxidation Characteristics Of Catechins In Suspended Fermentation Of Different 2 Varieties' Tea Leaves*. https://ssrn.com/abstract=4871586

Yogini S. Jaiswal, Pratima A. Tatke, Satish Y.Gabhe and Ashok B. Vaidya. (2010). Isolation and Quantitative Analysis of a Bioactive Polyphenol - Catechin in *Anacardium occidentale* Linn. (Leaves and Testa) by HPLC Analysis.