

ANTI-INFLAMMATORY ACTIVITIES OF *PEPEROMIA PELLUCIDA* [L.] KUNTH.: A REVIEW

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ABSTRACT

Background: Inflammation is a natural body response, but when it reaches the systemic chronic inflammation stage, it can cause more dangerous complications. Many natural ingredients have been developed as anti-inflammatory agents. One of them is sirih bumi (*Peperomia pellucida* [L.] Kunth). **Objective:** This study aims to summarize and examine the research results related to the anti-inflammatory activity of the sirih bumi. **Methods:** Research articles were collected from various online databases such as Google Scholar, Google, Medline, Pubmed, and Science Direct. Inclusion and exclusion criteria were applied to obtain original research articles relevant to the desired topic, published in the last ten years, the full text was accessible, and the research methods and results were well explained and valid. **Results:** In total, only six articles are eligible to be discussed. The research was conducted in Indonesia, Nigeria, and Malaysia. In vitro and in vivo methods with various models and parameters were used to test the anti-inflammatory activity. All parts of the plant are proven to have anti-inflammatory effects that can be presented in extracts or herbal teas. The activity of sirih bumi is determined by the dose or concentration of administration, processing process, and harvest time. The combination with other samples must be reconsidered to maintain the desired anti-inflammatory effect. **Conclusion:** Anti-inflammatory activity of sirih bumi has been proven through various studies. The development of the sirih bumi product is expected to help handle inflammation and other diseases related to inflammation.

Keywords : peperomia pellucida, inflammation, extract, tea

INTRODUCTION

Inflammation is normal because it is the body's natural response to defend against infection and injury. However, inflammation still needs particular attention, especially if it has reached the stage of chronic systemic inflammation. This condition can induce and exacerbate various diseases such as cancer, diabetes mellitus, cardiovascular disease, neurodegenerative disorders, and autoimmune diseases. When it reaches this stage, disability and even death can

occur^[1,2]. Therefore, potential agents are needed to cure or prevent inflammation.

Many drugs have been developed to treat inflammatory conditions. Currently, the community uses both modern medicines and traditional herbal medicines. Many plants have been studied to treat inflammation. One of the plants that have the potential for efficacy and economics is sirih bumi (*Peperomia pellucida* [L.] Kunth).

Sirih bumi has not been widely cultivated so it is only considered as a

weed. This plant is known to have many pharmacological activities, including anti-inflammatory^[3-9]. This article summarizes and discusses the latest research developments related to sirih bumi as an anti-inflammatory agent.

METHODS

Search and Identification Stage

Google Scholar and four other electronic databases, such as Pubmed and Science Direct, were used as search engines. The search process was carried out until the end of May 2022. The search keywords used were "peperomia pellucida", "inflammatory", "cytokine", "edema", and the word in the Indonesian version.

Eligibility Selection

The first stage is the identification stage. The author searches for related articles online using predefined keywords. The title and abstract of the original article were assessed according to keywords. The second step is to filter the abstracts from the articles obtained. Only articles with abstracts that meet the specified eligibility criteria are then downloaded in their

entirety for the third stage, which is to determine the eligibility criteria in terms of content.

The inclusion criteria in this study were original research in original articles published in the last ten years. The type of research is not limited. If the article meets all the inclusion criteria, but the test results are not clearly reported, and the text cannot be accessed entirely and free of charge, the article will be excluded.

Extraction and Synthesis Data

Data were extracted into categories: year of publication, country of origin of authors, type of research, type of sample, plant parts used, and test parameters. Data is presented in tabular form.

Data Presentation

The data obtained are presented descriptively.

RESULTS

The stages of searching for research articles can be seen in Figure 1. The number of articles found is quite large for research on the anti-inflammatory activity of sirih bumi.

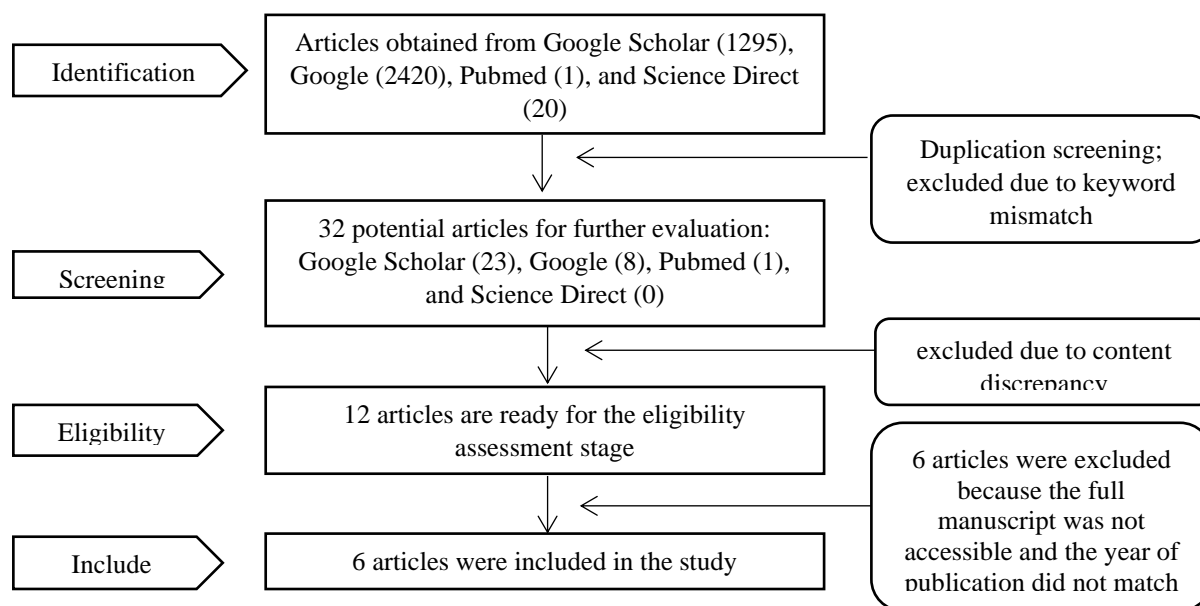


Figure 1. Schematic of browsing and selecting articles.

Table 1. Description of research data on the inflammatory activity of the sirih bumi

No.	Year of publication	Country origin of authors	Type of research	Type of samples	Plant parts	Test parameters	Reference
1.	2012	Indonesia	In vitro	Ethanol extract with red ginger	Whole Plant	Cox-2 inhibition	[11]
2.	2012	Indonesia	In vivo	Infusion	Herb	Volume of the foot paw	[12]
3.	2014	Indonesia	In vitro	Methanol extract	Whole plant	% cytokines inhibition	[13]
4.	2021	Indonesia	In vivo	Ethyl acetate and ethanol extract	Herb	Number of polymorphonuclear cells	[9]
5.	2021	Nigeria	In vitro	Methanolic extract	Fresh vegetables (stem and leaf)	% membrane stability and inhibition of protein denaturation	[14]
6.	2021	Malaysia	In vitro	Herbal tea	Stems and leaves	Anti-arachidonate 5-Lipoxygenase and antihyaluronidase activities	[10]

Six research articles that matched the search criteria and were available in the full text were analyzed further. The data that has been summarized are presented in table 1.

Many studies have been carried out on the anti-inflammatory activity of the sirih bumi. In the last ten years, six related studies have been found. Research with sirih bumi seems to still interest to researchers today. This can be seen from the number of publications in the last two years.

Table 1 shows that Indonesia is the country that has carried out the most research. This is probably due to the abundance of sirih bumi that can grow in Indonesia throughout the year. Research into the cultivation of this plant has been carried out to obtain better results than just taking it from the wild^[15]. In Indonesia, as a tropical country, many sirih bumi grow well in yards, rocky areas, and rice fields so that large-scale cultivation is relatively easy.

The type of research carried out is mostly in vitro studies. This is likely due to efficiency in time, cost, and the number

of samples that must be used. However, not a few in vivo studies have been carried out. Previously in 2004, the ethanolic extract of the sirih bumi was found to significantly reduce the volume of the foot paw and the number of leukocytes in an experiment using rats^[16]. Moreover, in 2010, petroleum ether extract significantly reduced carrageenan-induced hind paw edema^[17].

Various types of samples from the sirih bumi plant have been tested. It has been tested in the form of extracts and in the form of herbal teas that are ready to be consumed. The type of extract tested in the last ten years is classified as a type of extract that tends to be polar and semi-polar. However, the non-polar extract was tested in the previous years and proved to be effective^[17]. The anti-inflammatory effect is not only shown by certain plant parts but all parts of the plant have also been shown to have anti-inflammatory effects.

In a study conducted by Sulistiyani et al. (2012), sirih bumi extract was proven to inhibit the cyclooxygenase-2 enzyme in vitro. At a 100 g/mL concentration, the

inhibitory power was 47.5%. This activity is even better than red ginger extract. When the two extracts were combined, the activity decreased. This finding indicates that there is antagonism between the two extracts.

The activity of sirih bumi has also been proven *in vivo* through research by Barung et al. (2012). Sirih bumi herb infusion at a concentration of 30% has been shown to have the ability equivalent to a standard drug, phenylbutazone, at a dose of 5.04 mg/200 g BW rats in reducing the volume of rat paw edema. Increasing the concentration of sirih bumi to 60% can increase the anti-inflammatory effect.

Sirih bumi's ability to inhibit the release of pro-inflammatory cytokines also contributes to its anti-inflammatory activity. In the study of Salim et al. (2014), sirih bumi extract at a concentration of 5 µg/mL was able to inhibit the release of TNF-α (3.9 ± 0.8), IL-1α ($29.5 \pm 2.31\%$), IL-1β ($18.5 \pm 5.4\%$), IL-6 ($19.6 \pm 1.2\%$), and IL-8 ($6.4 \pm 1.0\%$) that involved in inducing acute inflammation. However, this activity was lower than the standard dexamethasone and andrographolide at the same concentration.

In the fourth article, sirih bumi was proven to reduce the number of PMN (polymorphonuclear) cells in experiments using rats. The number of PMN cells in the post-extraction tooth socket area decreased with the administration of both ethanol and ethyl acetate extracts. The inflammatory process that proceeds faster is thought to accelerate the recruitment of bone cells so that post-extraction tooth socket healing can run faster than the duration of healing through normal physiological processes^[9].

Drying the stems and leaves of the sirih bumi did not eliminate its anti-inflammatory effect. This phenomenon is founded on the study of Fakayode et al. (2021), who tested anti-inflammatory activity through membrane stabilization and inhibition of protein denaturation. The anti-inflammatory activity was more

excellent in the dry sample extract than in the fresh sample extract at the same concentration.

Experiments conducted by Ng et al. (2021) using the herbal tea of sirih bumi recommended the best drying process to optimize the anti-inflammatory effect of freeze-drying for unfermented and fully fermented sirih bumi products. As for the partially fermented sirih bumi, it is better to use hot air-dried.

The anti-inflammatory activity of sirih bumi is affected by the drying process and the time of harvest. Especially for the sirih bumi plant grown in subtropical countries, the optimum anti-inflammatory effect was found in plants harvested during phenophases 1 and 2 of winter and spring^[18].

The anti-inflammatory activity of sirih bumi is thought to come from dillapiol compounds. Dillapiol was found to have moderate antiphlogistic properties, so it can be used as a prototype for newer anti-inflammatory compounds. This activity is thought to be caused by the presence of the benzodioxole ring and alkyl groups in the side chain and the methoxy groups in the aromatic ring^[19]. Compounds with a similar structure in the sirih bumi may also be responsible for the emergence of anti-inflammatory activity in the sirih bumi.

CONCLUSION

Anti-inflammatory activity of sirih bumi has been tested in various countries, including Indonesia. In the last ten years, there have been six related studies published. The anti-inflammatory activity was tested both *in vitro* and *in vivo* using various products from sirih bumi. Sirih bumi is proven to have an anti-inflammatory effect determined by the dose or concentration of administration, processing process, and harvest time. The combination with other samples needs to be reconsidered to maintain the desired anti-inflammatory effect of sirih bumi.

CONFLICT OF INTEREST

There is no conflict of interest.

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REFERENCES

1. Furman D. Chronic inflammation in the etiology of disease across the life span. *Nature Medicine*. 2019;25:11.
2. Hunter P. The inflammation theory of disease. *EMBO Rep*. November 2012;13(11):968–70.
3. Kartika IGAA, Insanu M, Safitri D, Putri CA, Adnyana IK. New update: traditional uses, phytochemical, pharmacological and toxicity review of *Peperomia pellucida* (L.) Kunth. *Pharmacology Online*. 2016;2016(2):30–43.
4. Putri CA, Kartika A, Adnyana IK. Preventive effect of *Peperomia pellucida* (L.) Kunth herbs on ovariectomy-induced osteoporotic rats. 1 Januari 2016;25:546–51.
5. Kartika IGAA, Riani C, Insanu M, Eljabbar LFD, Adnyana IK. Sasaladaan (*Peperomia pellucida* [L.] Kunth.) Extracts Improve Trabecular Bone Microarchitecture in Ovariectomy-Induced Osteoporotic Rats. *International Journal of Green Pharmacy (IJGP)*. 2018;12(04):S1–6.
6. Kartika IGAA, Bang IJ, Riani C, Insanu M, Kwak JH, Chung KH, dkk. Isolation and Characterization of Phenylpropanoid and Lignan Compounds from *Peperomia pellucida* [L.] Kunth with Estrogenic Activities. *Molecules*. Januari 2020;25(21):4914.
7. I Gusti Agung Ayu Kartika, Muhamad Insanu, Catur Riani, Kyu HC, Adnyana IK. Polarity difference and the presence of phytoestrogen compounds affecting estrogenic activity of *Peperomia pellucida* extracts. *Sains Malaysiana*. Februari 2021;50(2):449–60.
8. Kartika A, Riani C, Insanu M, Paiboonsukwong K, Charoenphandhu N, Tubsuwan A, dkk. Potent Inhibition Of *Peperomia pellucida* Extracts Towards Rankl-Induced Osteoclast Formation Through M1 Macrophage Polarization. *Rasayan Journal of Chemistry*. 1 Januari 2021;14:1369–77.
9. Kartika IGAA, Riani C, Insanu M, Adnyana IK. *Peperomia pellucida* extracts stimulates bone healing in alveolar socket following tooth extraction. *J Tradit Complement Med*. 19 Agustus 2021;12(3):302–7.
10. Ng ZX, Than MJY, Yong PH. *Peperomia pellucida* (L.) Kunth herbal tea: Effect of fermentation and drying methods on the consumer acceptance, antioxidant and anti-inflammatory activities. *Food Chemistry*. 15 Mei 2021;344:128738.
11. Sulistiyani, Rahmania S, Husnawati. Potensi Campuran Ekstrak Suruhan (*Peperomia Pellucida*) Dan Jahe Merah (*Zingiber officina/E*) Sebagai AntlInflamasi Secara In Ftro. 2012 [dikutip 30 Mei 2022]; Tersedia pada: <http://repository.ipb.ac.id/handle/123456789/76091>
12. Barung EN, Wullur AC, Pansariang I. Uji Efektivitas Antiinflamasi Infus Herba Suruhan (*Peperomia Pellucida* L.) Pada Tikus Putih (*Rattus Norvegicus*). *JIF*. 2012;3(2):96541.
13. Salim E, Kumolosasi E, Jantan I. Inhibitory effect of selected medicinal plants on the release of pro-inflammatory cytokines in lipopolysaccharide-stimulated human peripheral blood mononuclear cells. *J Nat Med*. Juli 2014;68(3):647–53.
14. Fakayode AE. Phytonutrients, Antioxidants And Anti-Inflammatory Analysis Of *Peperomia Pellucida*. *JMPAS*. 15 Oktober 2021;10(5):3517–23.

15. Puluhalawa YA, Kandowanko NY, Solang M. Pupuk Terhadap Kandungan Proksimat dan Mineral pada Suruhan *Peperomia pellucida*. *Agrosains: J Penelit Agron*. 23 November 2021;23(2):60.
16. Wijaya S, S. W. M. Uji Efek Antiinflamasi Ekstrak Herba Suruhan (*Peperomia Pellucida* L. Kunth) Pada Tikus Putih Jantan. 2004;9:115–8.
17. Mutee AF, Salhimi SM, Yam MF, Lim CP, Abdullah GZ, Ameer OZ, dkk. In vivo anti-inflammatory and in vitro antioxidant activities of *Peperomia pellucida*. 2010;6(5):686–90.
18. Arrigoni-Blank M de F, Oliveira RLB, Mendes SS, Silva P de A, Antonioli AR, Vilar JC, dkk. Seed germination, phenology, and antiedematogenic activity of *Peperomia pellucida* (L.) H. B. K. *BMC Pharmacol*. 9 Mei 2002;2:12.
19. Parise Filho R, Pastrello M, Camerlingo C, Silva G, Agostinho L, Souza T, dkk. The anti-inflammatory activity of dillapiole and some semisynthetic analogues. *Pharmaceutical biology*. 1 November 2011;49:1173–9.