

ACTIVITY OF BAY LEAF EXTRACT (*Eugenia polyantha*) AS ANTI-INFLAMMATORY IN WHITE RAT (*Rattus norvegicus*): NARRATIVE REVIEW

Ida Ayu Nadia Kusumastuti^{1*}, Made Krisna Adi Jaya¹

¹Department of Pharmacy, Faculty of Math and Science, Udayana University, Bali, Indonesia

Corresponding author email: c.nadiakusuma9@gmail.com

ABSTRACT

Background: Inflammation is the body's defense response against foreign body invasion, tissue injury, or both caused by microorganisms, mechanical trauma, chemical compounds, and physical factors. Anti-inflammatory agents can be used to treat inflammation. Bay leaves are one example of a plant that can be used. Ethanol extract and water extract of a bay leaf can be anti-inflammatory because they contain flavonoids. **Objectives:** The purpose of this study was to see how effective ethanol extract and aqueous extract of bay leaf were as anti-inflammatory agents in mice. **Methods:** This study employs a systematic literature review approach, descriptive qualitative research, and library research. **Results:** The most efficacious dose was 150 mg/kg BW at a 70 percent concentration and at an 80 percent concentration for ethanol extract of bay leaves, and 50 mg/kg BW for the aqueous extract of bay leaves. **Conclusion:** Based on the results of this study, it can be concluded that bay leaf (*Eugenia polyantha*) ethanol extract and aqueous extract have anti-inflammatory activities **Keywords:** Anti-inflammatory, Bay Leaf, Diclofenac sodium, Ethanol Extract, Aqueous

INTRODUCTION

Indonesia has a tropical climate and the world's second-largest biodiversity after Brazil. It contains between 25,000 and 30,000 plant species, accounting for about 80 percent of all plant species in the world and 90 percent of plant species in Asia, and is widely utilized in traditional medicine^[2]. There has been a global trend to return to nature (back to nature) in the last decade, despite the availability of many types of modern medicine and the creation of new types of modern medicine. As a result, alternative medicines are becoming more popular and their use is expanding. Bay leaf is one of the plants that can be utilized as an anti-inflammatory treatment in Indonesia. In several studies, bay leaf (*Syzygium polyanthum* Wight.) has been found to contain a variety of compounds, including tannins, flavonoids, and essential oils

including citric acid and eugenol. Chemical compounds with anti-inflammatory activities are flavonoids, according to numerous research findings.

Bay leaf (*Syzygium polyantha*) is a type of spice that is familiar to most Indonesians. Besides being used as a flavoring in food, bay leaves can be used as an anti-inflammatory. Bay leaf plants are classified as follows:

Kingdom	:Plantae
Subkingdom	:Tracheobionta
Super divisi	:Spermatophyta
Divisi	:Magnoliophyta
Kelas	:Magnoliopsida
Sub kelas	:Rosidae
Ordo	:Myrtales
Famili	:Myrtaceae
Genus	: <i>Syzygium</i>
Spesies	: <i>Syzygium polyanthum</i>
(Wight.) Walp	^[14] .

The *Syzygium polyanthum* tree is about 25 meters high, and has large straight roots, a rounded trunk, and a smooth surface. It has small flowers, white and fragrant. While the leaves have a length of 2.5-8 cm with flat edges, blunt ends and wide at the bottom with a long and tight ^[18].

Inflammation is a normal response to the body's defenses to eliminate pathogens, prevent tissue damage from spreading, and heal damaged tissue as a result of disease pathological symptoms. If inflammation is not managed and occurs at the wrong time and in the wrong place, it can disrupt the body's homeostatic balance, lead to chronic inflammation, or harm tissue ^[12]. Rubor (redness), calor (heat), dolor (pain), tumor (swelling), and reduced function are all characteristics of the inflammatory response^[3]. Anti-inflammatory is defined as drugs that have an activity to suppress or reduce inflammation. Based on the mechanism of action, anti-inflammatory drugs are divided into two groups, namely steroid anti-inflammatory drugs and non-steroidal anti-inflammatory drugs. The mechanism of action of steroid and non-steroidal anti-inflammatory drugs mainly works to inhibit the release of prostaglandins into injured tissues^[5].

Based on research by Liliwirianis ^[10] bay leaves contain alkaloids, saponins, steroids, phenolics, and flavonoids. Meanwhile, based on research by Pinatih ^[14], bay leaves show the presence of flavonoid, terpenoid, and phenolic compounds. The anti-inflammatory ability of bay leaf infusion is influenced by the flavonoid compounds contained in it. Flavonoids are one of the important secondary metabolites in plants. Flavonoids are a type of secondary metabolite found in plants. Flavonoids are polyphenolic substances that help the body's defensive system by acting as an antiviral, antibacterial, antiallergic, antiplatelet, anti-inflammatory, anticancer, and antioxidant^[6]. Bay leaves include the flavonoids quercetin and flurethin ^[15].

Flavonoids' ability to prevent the production of histamine (one of the mediators of inflammation) is the mechanism by which inflammation is inhibited. Histamine release is inhibited, due to a reduction in inflammation ^[17]. Flavonoids can inhibit cyclooxygenase or lipoxygenase ^[8] as well as the buildup of leukocytes in the area, resulting in them being anti-inflammatory^[13]. The efficiency of bay leaf ethanol extract and aqueous extract as an anti-inflammatory in rats was compared to that of diclofenac sodium as a positive control in this study.

Chemical anti-inflammatory drugs are widely used by the public because they have a rapid effect in eliminating inflammation but also have the risk of dangerous side effects such as disorders of the gastrointestinal tract, blood, respiration, metabolic processes, hypersensitivity, and Reye's syndrome ^[16]. Diclofenac sodium is a non-steroidal anti-inflammatory drug (NSAID) with analgesic, anti-inflammatory, and antipyretic effects. Diclofenac sodium is an NSAID with high potency and good tolerance^[11]. Sodium 2-(2-((2,6-dichlorophenyl) amino) phenyl)acetate or often called sodium diclofenac is one of the drugs that has the potential to be developed as a candidate for COX inhibitors. Diclofenac sodium is a non-selective NSAID, acetic acid group, and a derivative of phenylacetic acid. This drug is a strong COX inhibitor with anti-inflammatory, analgesic and antipyretic effects. Diclofenac sodium has COX-inhibiting activity through inhibiting the formation of prostaglandins which are pain mediators, so it can be used to treat all kinds of pain, migraines and gout^[9].

METHODS

This study employs a systematic literature review approach, descriptive qualitative research, and library research. The primary and secondary data sources used in this literature are the findings of research published in national and

international journals. The selection of journals used as a library is done in database 1). Google Scholar, 2). Pubmed which are journals that have been chosen based on certain criteria. The articles are then gathered and saved on a storage device, which researchers may access. This study aims to determine the anti-inflammatory effect of ethanol extract and aqueous extract of bay leaf (*Eugenia polyantha*) on rats (*Rattus norvegicus*). The preparation procedure begins when all of the papers or journals have been collected.

RESULTS

1. Utilization of Bay Leaf Plants (*Eugenia polyantha*)

The bay plant (*Syzygium polyanthum*) from the Myrtaceae family is used as an anti-inflammatory in East Kalimantan, where it includes one of the flavonoid chemicals. Flavonoid compounds are known to have an anti-inflammatory effect whose mechanism of action is thought to inhibit the cyclooxygenase pathway in the arachidonic acid metabolic pathway. The leaves of the Indian bay leaf also contain flavonoid compounds. Other compounds include saponins, alkaloids, terpenoids, steroids, and antioxidants like tocopherol, β -carotene, and lutein, in addition to flavonoids [2]. Bay leaves contain dyes, tannins and essential oils which are antibacterial. The tannins contained are astringent. Benefits of leaves traditionally, bay leaves are used as a stomachache medicine. Bay leaves can also be used to help with constipation. Gout, stroke, high cholesterol, poor blood circulation, stomach irritation, itching, and diabetes can all be treated with bay tree [6].

2. Extraction and Compounds of Bay Leaf Plants (*Eugenia polyantha*)

Based on research conducted by Agustina [1], bay leaves were extracted using a 70 percent ethanol solvent and maceration for 3-5 days. Filtered and

stored in a container using filter paper. The bay leaf extract was then concentrated using a rotary evaporator and dried over a water bath. Bay leaves have flavonoids in their chemical components. According to Cahyaningsih [2]. Bay leaves were extracted by maceration process using 80 percent ethanol solvent for 1 day, stirring every day. The maceration process was repeated three times, and the immersion product was then filtered via a Buchner funnel. The extract was then concentrated in a 40°C oven to produce a thick extract. According to Hasanah and Nurul [7] 500 g of bay leaf *Simplicia* powder was extracted using the infundation method, which was heated with a water solvent over a water bath at a temperature of 95°C for 15 minutes, then filtered, and the infusion was evaporated after getting the infusion from the infundation returning to a water bath in order to get a thick extract with a consistent weight [4].

Table 1. Average Volume inflammation of White Rat [1]

Treatment	Volume of inflammation hourly				
	1	2	3	4	5
50 mg/kgBW	0,13	0,21	0,28	0,21	0,16
150 mg/kgBW	0,11	0,20	0,29	0,20	0,13
250 mg/kgBW	0,19	0,30	0,30	0,27	0,23
Na Diklofenac	0,08	0,24	0,19	0,18	0,16
Na CMC	0,22	0,30	0,32	0,34	0,38

Table 2. Dosage and Solvent

NO	Plant	Solvent	Dose used		
1	Bay Leaves	70% ethanol	50 mg/kg BW	150 mg/kg BW	250 mg/kg BW
	2	Indian Bay Leaves	80% ethanol	50 mg/kg BW	150 mg/kg BW
3		Bay Leaves	Aqueous	50 mg/kg BW	100 mg/kg BW

DISCUSSION

Anti-inflammatory Activity of Bay Leaf Plant (*Eugenia polyantha*)

Based on research conducted by Agustina,^[1] this study aims to determine the anti-inflammatory activity of ethanolic extract of bay leaves in terms of volume reduction of the soles of male white rats induced by carrageenan 1 percent. The measurement of the volume of edema on the soles of the rats' feet was carried out every hour for 5 hours after the rats' soles were inflamed by carrageenan induction. Observations for 5 hours were carried out to determine the time at which the maximum inflammation volume was formed. In this study, the mean volume of inflammation in the negative control group increased from the first hour to the fifth hour, where the largest inflammation volume occurred at the fifth hour.

Anti-inflammatory activity was measured using five separate experimental animal groups, including three test groups, one positive control group, and one negative control group. Bay leaf extract was administered to the test group, diclofenac sodium was provided to the positive control group, and CMC–Na was given to the negative control group. The bay leaf extract was administered in three doses: 50mg/kg BW, 150mg/kg BW, and 250mg/kg BW. Three doses of ethanol extract of bay leaf were found to be effective in decreasing inflammation. The test material was given orally 30 minutes before being induced with 0.1 mL of 1% carrageenan. The three doses of ethanol extract of bay leaf were able to inhibit inflammation. The volume of inflammation in the paws of rats which was smaller than the negative control group indicated that the ethanolic extract of bay leaves was able to suppress inflammation caused by carrageenan. The ethanolic extract of bay leaves was effective to inhibit inflammation caused by carrageenan, as evidenced by the lower volume of inflammation in the paws of rats compared to the negative control group.

The volume of inflammation appears to differ between the negative control group and the dose of ethanol extract of bay leaf.

The volume of inflammation increased from the first to the fifth hour in the negative control group given CMC–Na. An increase in the volume of inflammation began in the first hour to the third hour in the treatment group at doses of 50 mg/kg BW, 150 mg/kg BW, and 250 mg/kg BW, and began to decrease in the fourth hour. The results showed that the ethanolic extract of bay leaves had an anti-inflammatory effect on male white rats at all doses, and the most effective dose of ethanolic extract at a concentration of 70% was at a dose of 150 mg/kg BW because the volume of inflammation obtained was the smallest. Bay leaf extract's anti-inflammatory activity was lower than diclofenac sodium. The volume of inflammation in the diclofenac sodium group increased from the first hour and decreased at the third hour. Bay leaf extract's anti-inflammatory activities are thought to be linked to the inhibition of cyclooxygenase production. Flavonoids are compounds found in bay leaf extract that are hypothesized to have an anti-inflammatory impact by inhibiting the cyclooxygenase enzyme in the arachidonic acid metabolic pathway.

As discussed by Cahyaningsih^[2], the experiment divided the test animals (rats) into five groups first with the negative control group receiving 0.5 percent CMC–Na suspension, the positive control group receiving 50 mg Diclofenac Sodium suspension, group 1 receiving a suspension of ethanol extract of Indian bay leaf at a dose of 50 mg/kg BW, while group 2 received a suspension of ethanolic extract of Indian bay leaf at a dose of 150 mg/kg BW. Lastly, group 3 received a suspension of ethanolic extract of Indian bay leaf at a dose of 250 mg/kg BW. The ethanol extract used is 80% ethanol extract. A solvent mixture of alcohol and water is a suitable solvent for almost all low molecular weight compounds, such as

saponins and flavonoids, because it is the best extraction solvent for them. The average percent edema of each test substance group was not as large as the percent edema in the negative control group, indicating that all doses of the test substance group had an anti-inflammatory effect. The proportion of edema in the negative control group that received CMC-Na 0.5 percent increased from the 2nd to the 5th hour, but in the positive control test group, the percentage of edema increased from the 2nd to the 4th hour and decreased in the 5th hour. Meanwhile, in the test substance group, the maximum percentage of edema occurred at the 3rd hour for the first, second, and third doses, and reduced at the 4th and 5th hours. Furthermore, at 150mg/kg BW, the average percent of edema was lower than at 50mg/kg BW and 250mg/kg BW. As can be observed from the highest percentage of inhibition, administration of Indian bay leaf ethanol extract at a dose of 150 mg/kg BW has a great ability to suppress edema.

According to Hasanah and Hidayah^[7], The anti-inflammatory impact was examined using aqueous extract of bay leaves at doses of 50 mg/kg, 100 mg/kg, and 200 mg/kg, as well as a comparator, namely the non-steroidal anti-inflammatory medicine diclofenac sodium at a dose of 6.3 mg/kg. Diclofenac sodium was used as a positive control. Induction of inflammation was carried out chemically using 1% carrageenan as a negative control, which was injected subplantar into the soles of the rats' paws as much as 0.1 ml. Diclofenac sodium has analgesic and antipyretic activity and has the potential for a strong anti-inflammatory effect with lower gastrointestinal irritation side effects when compared to indomethacin, naproxen, and piroxicam. It was found that the percentage of inflammation inhibition in the comparison group with the EADS test group at all doses did not show a significant difference ($P>0.05$) at 30 minutes. Around minutes 120 and 180, the

EADS 50 mg/kg BW and 100 mg/kg BW groups differed significantly from the control group ($P>0.05$), in comparison to EADS 100 mg/kg BW and 200 mg/kg BW. This reveals that EADS 50 mg/kg BW is the most effective anti-inflammatory dose. Diclofenac sodium works by preventing the synthesis of prostaglandins by inhibiting the cyclooxygenase enzyme. Following oral treatment, diclofenac sodium is promptly and completely absorbed. The drug's plasma concentration is attained in 2-3 hours. Flavonoids, tannins, eugenol, and citric acid are among the chemical substances found in bay leaves. Flavonoids are compounds that have anti-inflammatory activities. Flavonoids have the ability to inhibit cyclooxygenase enzymes, lipoxygenases, and leukocyte buildup. This is in conformity with the results of this study's phytochemical screening of *Simplicia* and aqueous extract of bay leaf, which revealed the presence of flavonoid compounds with anti-inflammatory activities.

CONCLUSION

Based on the results of this study, it can be concluded that the ethanolic extract of bay leaves (*Eugenia polyantha*) can provide an anti-inflammatory effect, with the most effective doses of 70 percent and 80 percent ethanol extract concentrations at 150 mg/kg BW, and the aqueous extract concentrations at 50 mg/kg BW. The use of a solvent mixture of alcohol and water is an ideal solvent because it is the best extraction solvent for almost all low molecular weight compounds such as saponins and flavonoids.

CONFLICT OF INTEREST

This paper was written independently. All authors disclose no financial or personal relationships with other people or organizations that could inappropriately influence the work.

ACKNOWLEDGMENTS

We thank lecturers and staff in the Department of Pharmacy, Faculty of Math and Science, Udayana University, Bali Indonesia, for the support in the implementation of research.

REFERENCES

1. Agustina R, Indrawati DT, Masruhin MA. Aktivitas Ekstrak Daun Salam (*Eugenia polyantha*) Sebagai Antiinflamasi pada Tikus Putih (*Rattus norvegicus*). *Journal Trop Pharm Chem*. 2015; 3 (2): 120-123. (1)
2. Cahyaningsih E, Yuda ESK, Susanthi IM. Uji Efek Antiinflamasi Ekstrak Etanol Daun Salam India (*Murraya koenigii* L) terhadap Tikus (*Rattus norvegicus*) Jantan yang Diinduksi Karagenan 1%. *Medicamento*. 2018; 4 (1): 25-31. (2)
3. Corwin EJ. *Handbook of Pathophysiology*. 3th ed Philadelphia :Lippincort Williams & Wilkins ; 2008. (3)
4. Depkes RI. *Parameter Standar Umum Ekstrak Tumbuhan Obat Edisi I*. Jakarta: Departemen Kesehatan RI ; 2000 (4)
5. Gunawan *Farmakologi dan Terapi edisi 5*. Jakarta : Departemen Farmakologi dan Terapeutik Fakultas Kedokteran-Universitas Indonesia; 2007.
6. Harisma K, Chusniatun. Pemanfaatan Daun Salam (*Eugenia polyantha*) sebagai Obat Herbal dan Rempah Penyedap Makanan. *Warta LPM*. 2016; 19 (2): 110-118. (5)
7. Hasanah F, Hidayah N. Uji Aktivitas Antiinflamasi Ekstrak Air Daun Salam (*Syzygium polyanthum* Wight.) Terhadap Tikus Wistar Jantan yang Diinduksi Drngan Karagenan 1%. *Journal Of Pharmaceutical And Science*. 2018; 1(1) : 16-22. (6)
8. Hidayati NAS, Listyawati, Setyawan AD. (Kandungan Kimia dan Uji Antiinflamasi Ekstrak Etanol Lantana camara L. pada Tikus Putih (*Rattus norvegicus* L.) Jantan. *Bioteknologi*. 2008; 5 (1): 10-17. (7)
9. Hutauruk T, Rosita A, Oktavianawati I. 2014. Sintesis Asam 2-(2-(n-(2,6-diklorofenil)-4 fluorobenzamida)fenil)asetat sebagai Kandidat Obat Penghambat COX (siklooksigenase). *E-journal Pustaka Kesehatan*. 2014 : 2(2); 215-220.
10. Liliwirianis N, Musa NLW, Zain WZWM, Kassim J, Karim SA. Preliminary Studies on Phytochemical Screening of Ulam and Fruit from Malaysia. *E- Journal of Chemistry*. 2011; 8 (1): 285-288.
11. Mangampa I, Nugroho TE. Pengaruh Pemberian Natrium Diklofenak Dosis 1,4 MG/KgBB dan 2,8 MG/KgBB terhadap Kadar Serum Kreatinin Tikus Wistar. *Media Medika Muda*. 2015; 4(4): 1004-1012.
12. Muller WA. Leukocyte-endothelial cell intractions in the inflammatory response. *Lab Investigation*. 2002; 521-534. (8)
13. Narande JM, Wulur A, Yudisira A. Uji Efek Antiinflamasi Ekstrak Etanol Daun Suri (*Dracaena angustifolia* Roxb) Terhadap Edema Kaki Tikus Putih Jantan Galur Wistar. *Pharmacon Jurnal Ilmiah Farmasi*. 2013; 2(3) : 14-18(9)
14. Pinatih GNI, Suryadhi NT, Santosa A, Muliarta. Phytochemical Content and Antioxidant Activity in Traditional Balinese Babi Guling Spices. *Indonesian Journal of Biomedical Sciences*. 2011; 5(2); 1-12.
15. Prahastuti S, Tjahjani S, Hartini E. The Effect Of Bay Leaf Infusion (*Syzygium Polyanthum* (Wight) Walp) To Decrease Blood Total Cholesterol Level In Dyslipidemia Model Wistar Rats. *Jurnal Medika Planta*. 2011; 1(4). (10)
16. Pramitaningastuti A S, Anggraeny EN. 2017. Uji Efektivitas Antiinflamasi Ekstrak Etanol Daun

- Srikaya (*Annona squamosa* L.) Terhadap Edema Kaki Tikus Putih Jantan Galur Wistar. *Jurnal Ilmiah Farmasi*. 2017; 13(1): 8-14.
17. Rizki MI, Hariandja EM. Review: Aktivitas Farmakologis, Senyawa Aktif, dan Mekanisme Kerja Daun Salam (*Syzygium polyantha*). *Perkembangan Terkini Sains Farmasi & Klinik* 5. 2015; 6 (7): 239-244. (11)
 18. Sumono A., Wulan A.S.D. 2008. The use of bay leave (*Eugenia polyantha* Wight) in dentistry. *Dental Journal*. 41(3).