2_Anti-inflammatory_Activities_Swandari_Paramita.pdf

by

Submission date: 15-Aug-2019 05:47AM (UTC+0700)
Submission ID: 1160180932
File name: 2_Anti-inflammatory_Activities_Swandari_Paramita.pdf (136.13K)
Word count: 5356
Character count: 28639

BIODIVERSITAS
Volume 18, Number 4, October 2017
Pages: 1556-1561

ISSN: 1412-033X
E-ISSN: 2085-4722
DOI: 10.13057/biodiv/d180434

Anti-inflammatory activities of ethnomedicinal plants from Dayak Abai in North Kalimantan, Indonesia

SWANDARI PARAMITA[1,♥], KHEMASILI KOSALA[1], DZULKIFLI DZULKIFLI[2], DEBY INDAH SAPUTRI[1], ENGGAR WIJAYANTI[3]

[1]Faculty of Medicine, Universitas Mulawarman. Jl. Kerayan Kampus Gunung Kelua, Samarinda 75119, East Kalimantan, Indonesia. Tel./Fax. +62-541-748581. ♥email: swandariparamita@gmail.com
[2]Faculty of Forestry, Universitas Mulawarman. Jl. Ki Hajar Dewantara Kampus Gunung Kelua, Samarinda 75119, East Kalimantan, Indonesia
[3]Center for Research and Development of Medicinal Plants and Traditional Medicine. Jl. Raya Lawu No.11 Tawangmangu, Karanganyar 57792, Central Java, Indonesia

Manuscript received: 18 November 2016. Revision accepted: 5 October 2017.

Abstract. *Paramita S, Kosala K, Dzulkifli D, Saputri DI, Wijayanti E. 2017. Anti-inflammatory activities of ethnomedicinal plants from Dayak Abai in North Kalimantan, Indonesia. Biodiversitas 18: 1556-1561.* Inflammation is a normal process in the human body as a response to injury from the healing process. Meanwhile, chronic inflammation will cause new health problems to patients. Anti-inflammatory drugs generally used for those conditions, have several side effects to patients. The objective of this research was to find alternative anti-inflammatory drugs, especially from natural sources. Three medicinal plants recorded from Dayak Abai in North Kalimantan, Indonesia for health problems caused by the inflammation process i.e. *Amomum xanthophlebium* Baker, *Clerodendrum buchananii* (Roxb.) Walp., and *Donax canniformis* (G.Forst.) K.Schum. were used as material in this research. The experimental method using carrageenan-induced rat paw edema was used followed by the resulting measurement using plethysmometer. The results showed that significant differences of AUC (area under the curve) with $p = 0.001$ ($p < 0.05$) were achieved between negative control, positive control, and treatment group with plant medicinal extracts. AUC of leaves ethanol extract of *C. buchananii* showed the strongest anti-inflammatory activities. It could be concluded that the medicinal plants recorded from ethnomedicinal data from Dayak Abai in North Kalimantan, have anti-inflammatory activities, with *C. buchananii* as the most potential ones which could be further developed as a new source of the anti-inflammatory drug.

Keywords: Anti-inflammatory, *Amomum xanthophlebium*, *Clerodendrum buchananii*, *Donax canniformis*, carrageenan-induced rat paw edema

INTRODUCTION

Inflammation is a physiological process in the body in response to a lesion on the body. Acute inflammation can be triggered by various stimuli which could be seen from the rapid response at the site of infected or damaged tissues such as leukocytes carriers and protein plasm (antibodies) to the site of inflammation. Chronic inflammation can occur due to the subsequent process of acute inflammatory processes from several weeks to months and even years. During the course of acute and chronic inflammation, a number of chemical mediators will be released. A large number of inflammatory mediators are released via arachidonic acid pathways, including prostaglandins, as a result of the breakdown of arachidonic acid by cyclooxygenase enzymes. Although inflammation is a physiological process in the body, it can cause severe impacts for patients, including the emergence of pain, swelling, fever and other symptoms (Souza et al. 2012).

To overcome these effects, most types of anti-inflammatory drugs are applied. There are two classes of anti-inflammatory drugs i.e. NSAIDs (non-steroidal anti-inflammatory drugs) and corticosteroids. NSAIDs work by inhibiting cyclooxygenase enzyme action. While corticosteroids will inhibit the expression of cyclooxygenase enzyme. The inhibition of inflammation process may help patients by: (i) Reducing inflammation process, especially for patients with the muscle injury and other conditions with swelling of the joints. (ii) Reducing pain, especially for patients with osteoarthritis, rheumatism, gout, surgery effects (Pountos et al. 2011). (iii) Reducing fever, mainly due to inhibition of prostaglandin production in the hypothalamus as the main role in the process of fever. (iv) Protecting the heart by inhibiting the production of thromboxane A2 enzymes in the clot formation process, which potentially cause blockages in coronary artery heart (Goodman et al. 2010).

In spite of many advantages, the use of anti-inflammatory drugs also has indisputable side effects. Some prominent side effects of anti-inflammatory drugs are the effects on the gastrointestinal system. This is mainly because the inhibition of cyclooxygenase enzymes, especially COX-1, will trigger the inhibition of prostacyclin and PGE2. In the stomach, prostacyclin and PGE2 are known as the protector of gastric wall mucosa from the effects of stomach acid. As a result, the side effects of those drugs appear such as nausea, severe vomit, and the hardest effects i.e. peptic ulcer with bleeding complications as the major cause of death. The use of high or long-term doses of NSAIDs, along with corticosteroids

and/or anticoagulants, smoking and/or alcohol, increases the risk of these side effects. In addition, some studies have reported that some NSAIDs also have direct destructive effects on gastric mucosal cells, causing these side effects (Siew and Francis 2010). Another side effect is on the cardiovascular system. Prostaglandins produced by the cyclooxygenase process regulate the complex interactions between platelets and blood vessel walls. In the administration of selective anti-inflammatory drugs COX-2, the imbalance production of prostacyclin and TXA2 occurs, leading to an imbalance of a prothrombotic in the blood, which further increases the risk of thrombotic blood events (Antman et al. 2007). Of these reasons, incessant efforts to find alternative anti-inflammatory drugs, especially those derived from natural materials are very important.

Indonesia is known as one of the mega-biodiversity countries with the abundance of medicinal plants. Each ethnic communities has a diverse culture and a local wisdom, including the use of plants for traditional medicine. Knowledge of the use of medicinal plants by indigenous communities is essential for the development of traditional medicine and the development of modern medicine. This is because most plant extracts used in modern medicine are found through local knowledge approach. The use of medicinal plant data from ethnobotany research is an effective way to discover new potential chemicals for treatment. Research on Local Knowledge Exploration of Ethnomedicine and Community-Based Drugs in Indonesia is also known as the Research of Medicinal and Herbs (*Riset Tumbuhan Obat dan Jamu* or RISTOJA) (MoH RI 2016).

The RISTOJA program of the Indonesian Ministry of Health undertaken in North Kalimantan in 2015 produced a number of identified-medicinal plant information up to the species level. This program also successfully recorded the indications/complaints of the disease, including the health problems caused by the inflammatory process. Around 25 medicinal plants with ethnomedicinal data showing anti-inflammatory effects had been recorded. Based on published papers, the comprehensive study of the anti-inflammatory activity of three medicinal plants i.e. *Clerodendrum buchananii* (Roxb.) Walp., *Donax canniformis* (G.Forst.) K. Schum., and *Amomum xanthophlebium* Baker is still limited (Ismail et al. 2012; Ismail et al. 2015; RIMU 2015). These were supported by ethnomedicinal data from Dayak Abai ethnic group in North Kalimantan. Therefore, the objective of this study was to test the anti-inflammatory activity of the three medicinal plants i.e. *Clerodendrum buchananii* (Roxb.) Walp., *Donax canniformis* (G.Forst.) K. Schum., and *Amomum xanthophlebium* Baker originated from Dayak Abai ethnic group in North Kalimantan.

MATERIALS AND METHODS

Sampling and sample identification

The sampling of medicinal plants was conducted at the location of RISTOJA 2015 research, i.e. Dayak Abai settlement in Sentaban Village, Malinau Barat Sub-district, Malinau District, North Kalimantan (MoH RI 2016). The plant sampling was located at about 900 km from Samarinda, the capital of East Kalimantan province. Plants were then be identified in the Laboratory of Ecology and Dendrology of the Faculty of Forestry, Mulawarman University, Samarinda, East Kalimantan, Indonesia to certify the plant legality. Based on the plant identification, the medicinal plants used in this study were *Amomum xanthophlebium* Baker., *Clerodendrum buchananii* (Roxb.) Walp., and *Donax canniformis* (G.Forst.) K. Schum. While, experimental research was conducted in This study was conducted in the Research Laboratory of the Faculty of Medicine, Mulawarman University, Samarinda, East Kalimantan, Indonesia.

Medicinal plant extractions

The extraction of medicinal plant followed the guidelines from the Indonesian Herbal Pharmacopoeia (MoH RI 2008). Medicinal plants were dried and then crushed into simplicia. The simplicia were then macerated using absolute ethanol solvent in a ratio of 1 part of simplicia to 10 parts of solvent. The mixture was soaked for 6 hours followed by stirring occasionally with an orbital shaker at room temperature in each interval hours, which were then stood for 18 hours. The mixture was then separated using filter paper, then evaporated with a rotary evaporator at 50°C. The obtained viscous extract was dried to obtain a dry extract. The dried extracts were then stored in a refrigerator of -20°C for further study.

Anti-inflammatory test activity

Anti-inflammatory activity of medicinal plant extracts was tested by carrageenan-induced rat paw edema method and measured using a plethysmometer. There were 5 groups of experimental animals in this study: (i) Group 1 was negative control; (ii) Group 2 was a positive control by giving indomethacin dose 10 mg/kg orally; (iii) Groups 3, 4 and 5 were treated with medicinal plant extracts in different doses. Each group consisted of 5 individuals.

The dosage of medicinal plants was determined using calculation table conversion for various species of animal species (Bacharach and Laurence 1964). Doses for *C. buchananii* was as follows: dosage I 0.91 mg/kg, dose II 1.81 mg/kg, and dosage III 3.63 mg/kg. Doses for *D. canniformis* was as follows: dosage I 0.54 mg/kg, dosage II 1.08 mg/kg, and dosage III: 2.16 mg/kg. Doses for *A. xanthophlebium* was as follows: dosage I 0.25 mg/kg, dosage II 0.5 mg/kg, and dosage III 1 mg/kg.

Carrageenan (0.1 ml of 1% in 0.9% NaCl) was injected in subcutaneous in left paw substrate of rat and waited the work reaction for an hour. After the injection, the volume of rat paw edema was measured with the plethysmometer. The measurement was further done at the 1st, 2nd, 3rd, 4th, 5th, and 6th hours after the injection. Paw edema is defined as the changes of the rat paw edema after the carrageenan injection on the left paw sub-plant measured by plethysmometer in a certain time range. Percentage of edema inhibition changes were calculated using the formula as follows: (V1-V0) x 100%, where V1 is the left

paw volume of the treated rats within a certain time range, V0 is the left paw volume of the rat before carrageenan injection (Eddouks et al. 2012).

Data analysis

The obtained data were calculated for each mean and SE (standard error) for the results of paw edema test. Obtained data was then statistically analyzed by ANOVA followed by Tukey post hoc, with the level of confidence at 95% ($p < 0.05$) using PSPPIRE 0.8.4. software. To compare anti-inflammatory activity among the three medicinal plants, the AUC (under curve area) was calculated from all the obtained results. All data were presented in tables and graphs.

RESULTS AND DISCUSSION

Anti-inflammatory activity of each medicinal plant

The results of the oral administration of the medicinal plants extract for the inhibition of rat paw edema induced by carrageenan are shown in Table 1. The effectivity of those medicinal plant extracts relative to the negative control and indomethacin used as positive control was also observed. It can be observed that the plant medicinal extract showed a significant antiedematogenic activity, within the first hour after the extracts administration; with ANOVA results indicated statistically significant differences between treatment ($p < 0.001$). The Tukey post hoc test showed a decrease in paw edema volume in the first hour after carrageenan injection, compared to the control group. The administration of *C. buchananii* extract with the dosage I produced a significant reduction in the paw edema after 1 h of extract application ($p < 0.05$). The same results were also shown in the application of *D. canniformis* extract with the dosage III ($p < 0.001$), and *A. xanthophlebium* extract with the dosage III ($p < 0.001$), which reduced the paw edema compared to the controls after 1 h of those extract administration. As expected, the reference drug, indomethacin (10 mg/kg), caused a significant inhibition of post-carrageenan edema.

Comparison of anti-inflammatory activity of three medicinal plants

Comparison of anti-inflammatory activity among three medicinal plants was observed based on the calculation of AUC values (area under the curve) from all research results. Table 2 shows the results of paw edema AUC with the administration of *C. buchananii*, *D. canniformis*, and *A. xanthophlebium*. There were significant differences of AUC results amongst three medicinal plants and controls with $p < 0.01$. The lower AUC score indicated that the prevalence of paw edema was less. The Tukey post hoc test showed significant differences in AUC score ($p < 0.05$) for *C. buchananii* dosage I, *D. canniformis* dosage III, and *A. xanthophlebium* dosage III when compared to the controls. Since the edema indicates an inflammatory process, when the prevalence of edema was less after it was administered by the extract of plant medicinal, it means that the activity of anti-inflammatory of the medicinal plant extract was very strong. The lowest AUC results of the three medicinal plants could be seen in the first dose of *C. buchananii* extract.

Table 1. Average of carrageenan-induced paw edema inhibition after the administration of plant extracts

Plants	Group	Average inhibition (mm3) ± SE per-hour						
		0	1	2	3	4	5	6
CB	Control	41.7 ± 3.8	36.6 ± 3.7	34.1 ± 4.4	31.8 ± 4.0	30.6 ± 4.1	29.0 ± 4.2	24.8 ± 3.8
	Indomethacin	76.9 ± 3.3*	71.0 ± 3.1	68.4 ± 3.8	62.8 ± 2.9	60.3 ± 2.5	54.4 ± 3.1	47.3 ± 2.1
	Dosage I	79.3 ± 8.3*	74.2 ± 2.3*	67.8 ± 2.3	61.7 ± 1.9	58.8 ± 1.5	54.0 ± 2.2	46.7 ± 1.8
	Dosage II	66.6 ± 3.6	55.4 ± 4.9	50.3 ± 3.4	44.9 ± 2.9	40.5 ± 3.2	36.6 ± 2.8	29.7 ± 2.2
	Dosage III	72.4 ± 10.3	48.5 ± 10.3	45.7 ± 7.9	43.2 ± 4.9	41.2 ± 5.0	38.8 ± 4.9	37.3 ± 3.9
DC	Control	41.7 ± 3.8	36.6 ± 3.7	34.1 ± 4.4	31.8 ± 4.0	30.6 ± 4.1	29.0 ± 4.2	24.8 ± 3.8
	Indomethacin	76.9 ± 3.3***	71.0 ± 3.1***	68.4 ± 3.8***	62.8 ± 2.9**	60.3 ± 2.5**	54.4 ± 3.1*	47.3 ± 2.1
	Dosage I	78.6 ± 8.3***	47.4 ± 2.3	41.2 ± 2.3	38.0 ± 1.9	34.6 ± 1.5	30.9 ± 2.2	27.8 ± 1.8
	Dosage II	74.2 ± 8.0***	57.1 ± 10.9	44.9 ± 7.6	39.6 ± 6.4	37.6 ± 7.0	34.4 ± 6.3	30.1 ± 4.8
	Dosage III	74.2 ± 9.1***	69.2 ± 10.2***	56.2 ± 7.6	47.0 ± 4.7	44.5 ± 5.1	41.7 ± 4.4	32.4 ± 3.5
AX	Control	41.7 ± 3.8	36.6 ± 3.7	34.1 ± 4.4	31.8 ± 4.0	30.6 ± 4.1	29.0 ± 4.2	24.8 ± 3.8
	Indomethacin	76.9 ± 3.3***	71.0 ± 3.1***	68.4 ± 3.8**	62.8 ± 2.9**	60.3 ± 2.5**	54.4 ± 3.1	47.3 ± 2.1
	Dosage I	85.2 ± 4.2***	72.1 ± 5.0***	61.1 ± 3.5*	56.8 ± 3.5	51.7 ± 3.8	44.4 ± 3.0	37.2 ± 3.0
	Dosage II	77.6 ± 8.2***	67.6 ± 7.9**	61.8 ± 7.3*	58.2 ± 6.9*	53.5 ± 6.0	47.7 ± 5.2	37.8 ± 4.8
	Dosage III	84.3 ± 3.8***	66.0 ± 5.6**	59.3 ± 4.3	53.9 ± 4.8	49.9 ± 6.4	45.3 ± 4.9	37.4 ± 5.1

Note: ANOVA (CB: *C. buchananii* $p<0.001$; DC: *D. canniformis* $p<0.001$; AX: *A. xanthophlebium* $p<0.001$), followed by Tukey post hoc test, with $^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$ compared to control

Table 2. The average AUC of carrageenan-induced paw edema inhibition after the administration of plant extracts

Group	AUC ± SE
Control	406.69 ± 23.50
Indomethacin	224.57 ± 14.63*
C. buchananii dosage I	224.16 ± 20.50*
C. buchananii dosage II	327.67 ± 25.85
C. buchananii dosage III	328.47 ± 66.46
D. canniformis dosage I	356.22 ± 9.61
D. canniformis dosage II	336.42 ± 14.66
D. canniformis dosage III	292.77 ± 30.66
A. xanthophlebium dosage I	256.20 ± 18.77*
A. xanthophlebium dosage II	258.41 ± 38.69*
A. xanthophlebium dosage III	268.69 ± 26.62

Note: ANOVA ($p<0.01$), followed by Tukey post hoc test, with *$p<0.05$ compared to control

Discussion

Our findings firstly highlight the potency of ethnomedicinal plants from Dayak Abai for anti-inflammatory properties, providing a scientific basis for the alternative uses of ethnomedicinal plants from Dayak Abai in the treatment of inflammatory disorders. The results of this study indicate that all three medicinal plants i.e. *C. buchananii*, *D. canniformis*, and *A. xanthophlebium* had anti-inflammatory effects, with *C. buchananii* leaf extract showed the strongest anti-inflammatory activity of all two other medicinal plants, based on carrageenan-induced paw edema test results.

Specifically, *C. buchananii* used in this study belongs to the *Lamiaceae* family. Dayak Abai ethnic group in Malinau District, North Kalimantan named it as "tengger asam". The leaves are mostly used as traditional medicine. *C. buchananii* is also used in some other places as a medicinal plant. As an example, *C. buchananii* in Serampas, Jambi, known also as "bungo panggil", was used for expelling the certain disease due to the superstitious practices (Hariyadi and Ticktin 2012). *C. buchananii* in Pekurehua, Central Sulawesi which is locally called as "lelimbanua", was used as a medication for shortness of breath, swelling or rheumatism (Susiarti et al. 2009). *C. buchananii* in Tobelo, North Maluku, also locally known as "tatabako", was used to treat sick people by boiling the leaves which were then drunk or rubbing the leaves applied to the body (Susiarti et al. 2015). *C. buchananii* in Kaulong, Papua New Guinea is called "cocoyat", its leaves are used to treat fungus infections and skin lesions (Prescott et al. 2012). *C. buchananii* in Roviana, Solomon Islands called "titimunuhaha", is also used as a traditional medicine there (Furosawa et al. 2014). Based on this many local information regarding with the use of *C. buchananii* in traditional medicine practices, we are interested to study this medicinal plant and; fortunately, we successfully confirmed that this medicinal plants had a high potency as anti-inflammatory medicines.

Several other species of *Clerodendrum* including *Clerodendrum infortunatum* L.; *Clerodendrum paniculatum* L.; *Clerodendrum phlomidis* L.f.; and *Clerodendrum volubile* P.Beauv have been studied their anti-inflammatory activities. *C. infortunatum*, for example, is used as a traditional medicine in India, Bangladesh, Pakistan and surrounding areas. *C. infortunatum* leaves were used as bronchitis and asthma drug in Bangladesh (Apu et al. 2012). One published study found the anti-inflammatory activity *in vitro* on ethanol extract of *C. infortunatum* leaf using the writhing test (peripheral analgesic effect) and the tail flick method (central analgesia effect) (Kale and Maniyar 2015; Chandrashekar and Rao 2013). Another study also reported that ethanol extract of *C. infortunatum* root using writhing method possessed a valuable anti-inflammatory activity (Sumi et al. 2015). The same founding of anti-inflammatory activity also reported on ethanol extract of *C. infortunatum* leaf using carrageenan-induced rat paw edema (Chandrashekar and Rao 2014). Interestingly, other natural compounds such as saponins were successfully isolated from *C. infortunatum* leaf showing analgesic activity with writhing test and hot plate test (Das et al. 2014).

Clerodendrum species which are also frequently studied their anti-inflammatory activity is *C. phlomidis*. This plant is also used as a traditional medicine in India, Bangladesh, Pakistan and surrounding areas, especially for joint pain medication. One study found that *C. phlomidis* leaf extract had anti-inflammatory and anti-arthritic activity using carrageenan-induced paw edema and arthritis induced with FCA (Freund complete adjuvant) in trial rats (Prakash et al. 2014). Other studies also reported the same founding in the root extract of *C. phlomidis* using granuloma cotton pellet method (Parekar et al. 2012). Interestingly, other published papers also found that *C. phlomidis* extracts had analgesic, antiasthma, and antiarthritic effects (Raja and Mishra 2010). Other *Clerodendrum* species, i.e. *C. volubile* have been also studied its anti-inflammatory activity which is mostly used as a traditional medicine in Senegal and surrounding areas, especially for joint pain medication. The presence of anti-inflammatory activity of *C. volubile* leaf extract was successfully found using rat paw edema induction method with fresh albumin (Adediwura and Yewande 2012). From all studies of anti-inflammatory activity of *Clerodendrum* species; however, the published research of *Clerodendrum* species in Indonesia associated with that activity was still limited. A study of *C. paniculatum* in North Sumatra found that anti-inflammatory activity could be obtained using granuloma cotton pellet method and the induction of rat paw edema with carrageenan (Hafiz et al. 2016). Therefore, we used the local *Clerodendrum* species originated from Dayak Abai ethnic group in Malinau District, North Kalimantan as our focus study and successfully confirm their potency as anti-inflammatory medicine which could be further developed.

We also used carrageenan-induced paw edema model in this study because it is a frequently used as the method for testing non-steroidal anti-inflammatory agents. Carrageenan is a linear sulfate polysaccharide derived from an edible seaweed species. Carrageenan is commonly used

in food and pharmaceutical industries because of its ability to form gels, as hardener and preservative. Carrageenan is widely used as a phlogistic agent to induce acute inflammation, and it is a classic model applied in research on NSAIDs. Besides being non-antigenic and having no systemic effect, carrageenan is known to produce a pro-inflammatory response. Edema caused by carrageenan injection is characterized by swelling of localized areas with fluid and leukocytes, resulting in swelling of the legs (Tasleem et al. 2014; Archera et al. 2015).

The formation of carrageenan-induced edema in rat paws is a biphasic event over a period of 1 to 5 hours. The initial phase (1 to 1.5 hours) is dominated by nonphagocytic edema, followed by a second phase with increased edema formation which occurred in the rest five hour. There are differences of mediators in various phases in carrageenan-induced edema. The initial phase (up to the first 1.5 hours) is characterized by the release of histamine, 5-hydroxytryptamine, PAF (platelet activating factor) and serotonin. Kinin is released from 1.5 to 2.5 hours in the last phase, the inflammation will continue until the fifth hour by lipid-derived eicosanoid (prostaglandin, leukotriene 5-hydroperoxyeicosatetraenoic acid, and others) (Ray et al. 2015; Cheng et al. 2016).

In carrageenan-induced paw edema, the following events occur (i) Induction of COX-2 and mPGES-1 during the ongoing production of PGE2 on swollen paws. (ii) Carrageenan-induced paw edema causes COX-2 upregulation and general improvement of prostanoids in the central nervous system during the early phases of inflammation. (iii) Peripheral inflammation causes a significant increase in PGE2 and selective induction of mPGES-1 in the central nervous system. (iv) Prostacyclin levels increase in the central nervous system during the early phase of carrageenan-induced paw edema without significant PGIS upregulation (Zhang et al. 2013; Erasalo et al. 2015). The action mechanism of medicinal plant extracts as the anti-inflammatory agent is predicted due to the flavonoid content of those plant extracts. Therefore, the three medicinal plants used in our study, might contain high flavonoid contents especially in *C. buchananii* leaf extract, which show the strongest anti-inflammatory activities. Although, the further secondary metabolite analysis may need to be intensively observed to confirm this flavonoid concentration. An important mechanism of anti-inflammatory activity is the inhibition of enzymes that produce eicosanoid, including A2 phospholipase, cyclooxygenase, and lipoxygenase, leading to the decrease concentration of prostanoid and leukotrienes. Other mechanisms include inhibition of histamine release, phosphodiesterase, protein kinase and transcriptase activation (Rathee et al. 2009).

In summary, our findings are the first scientific report to show the potency of ethnomedicinal plants from Dayak Abai as anti-inflammatory medicine using the carrageenan-induced paw edema model. Our study finds that there were significant differences in anti-inflammatory activity of amongst treated medicinal plants (*C. buchananii, D. canniformis* and *A. xanthophlebium* extracts) compared to the negative control and positive control using carrageenan-induced paw edema method with $p < 0.001$. The extract of *C. buchananii* had the ability to inhibit the paw edema stronger than that of other two medicinal plants. Based on the findings of this study, we suggest that more research in this area especially on the secondary metabolite analysis should be further developed due to the high potency of this medicinal plants as a new anti-inflammatory agent based on natural materials.

ACKNOWLEDGEMENTS

This study was funded by the Center for Research and Development of Medicinal and Traditional Medicinal Plants, Indonesian Health Research and Development Agency, Ministry of Health, as part of the implementation of the Advanced Research of Local Ethnomedicine and Local Community-Based Scientific Research Exploration in Indonesia 2016.

REFERENCES

Adediwura FJ, Yewande A. 2012. Pharmacognostic studies and antiinflammatory activities of *Clerodendrum volubile* P Beauv Leaf. Intl J Phytomed 4: 414-418.

Antman EM, Bennet JS, Daugherty A, Furberg C, Roberts H, Taubert KA. 2007. Use of nonsteroidal anti-inflammatory drugs: An update for clinicians. A scientific statement from the American Heart Association. Circulation 115 (12): 1634-1642.

Apu AS, Bhuyan SH, Prova SS, Muhit MA. 2012. Anti-inflammatory activity of medicinal plants native to Bangladesh: A review. J Appl Pharmaceut Sci 2 (2): 7-10.

Archera AC, Muthukumar SP, Halami PM. 2015. Anti-inflammatory potential of probiotic *Lactobacillus spp*. on carrageenan induced paw edema in *Wistar* rats. Intl J Biol Macromol 81: 530-537.

Bacharach DR, Laurence AL. 1964. Evaluation of Drug Activities: Pharmacometrics. Academic Press, Cambridge, MA.

Bhattacherjee D, Das A, Das SK, Chakraborthy GS. 2011. *Clerodendrum infortunatum* Linn.: A review. J Adv Pharm Healthcare Res 1 (3): 82-85.

Chandrashekar R, Rao SN. 2013. Chronic central and peripheral analgesic activity of extract of the leaves of *Clerodendrum viscosum* in rodent models. Intl J Appl Biol Pharmaceut Technol 4 (1): 58-62.

Chandrashekar R, Rao SN. 2014. Chronic anti-inflammatory activity of ethanolic extract of leaves of *Clerodendrum viscosum* by carrageenin induced paw oedema in *Wistar* albino rats. Br J Pharmaceut Res 3 (4): 579-586.

Cheng J, Ma T, Liu W, Wang H, Jiang J, Wei Y, Tian H, Zou N, Zhu Y, Shi H, Cheng X, Wang C. 2016. In in vivo evaluation of the anti-inflammatory and analgesic activities of compound Muniziqi granule in experimental animal models. BMC Compl Altern Med 16 (20): 1-10.

Das B, Pal D, Haldar A. 2014. A review on biological activities and medicinal properties of *Clerodendrum infortunatum* Linn. Intl J Pharm Pharmaceut Sci 6 (10): 41-43.

Eddouks M, Chattaopadhyay D, Zeggwagh NA. 2012. Animal models as tools to investigate antidiabetic and anti-inflammatory plants. Evid-Based Compl Altern Med. ID 142087: 1-14. DOI: 10.1155/2012/142087.

Erasalo H, Laalova M, Hamalainen M, Leppanen T, Nieminen R, Moilanen E. 2015. PI3K inhibitors LY294002 and IC87114 reduce inflammation in carrageenan-induced paw oedema and down-regulate inflammatory gene expression in activated macrophages. Basic Clin Pharmacol Toxicol 116: 53-61.

Furosawa T, Sirikolo MQ, Sasaoka M, Ohtsuka R. 2014. Interaction between forest biodiversity and people's use of forest resources in Roviana, Solomon Islands: implications for biocultural conservation under socioeconomic changes. J Ethnobiol Ethnomed 10 (10): 1-20.

Goodman LS, Brunton LL, Chabner B. 2010. Goodman & Gilman's The Pharmacological Basis of Therapeutics. McGraw-Hill Medical, New York.

Hafiz I, Rosidah, Silalahi J. 2016. Antioxidant and anti-inflammatory activity of pagoda leaves (*Clerodendrum paniculatum* L.) ethanolic extract in white male rats (*Rattus novergicus*). Intl J PharmTech Res 9 (5): 165-170.

Hariyadi B, Ticktin T. 2012. Uras: Medicinal and Ritual Plants of Serampas, Jambi Indonesia. Ethnobot Res Appl 10: 133-149.

Ismail S, Mujiono K, Taufik I, Razaki HA, Merry. 2012. Research on Local Ethnomedicine and Medicinal Knowledge Exploration in Indonesia: Community-Based in East Kalimantan. Agency for Health Research and Development, Ministry of Health, Jakarta. [Indonesian]

Ismail S, Suwasono RA, Supriyoko W, Kuswanto H, Paryono. 2015. Research on Local Ethnomedicine and Medicinal Knowledge Exploration in Indonesia: Community-Based in the Abai Tribe of Malinau District, North Kalimantan Province. [Research Report]. Agency for Health Research and Development, Ministry of Health, Jakarta. [Indonesian]

Kale A, Maniyar YA. 2015. Evaluation of peripheral and central analgesic activity of ethanolic extract of *Clerodendrum infortunatum* Linn. in experimental animals. Intl J Basic Clin Pharmacol 4 (5): 912-918.

MoH RI. 2008. Indonesian Herbal Pharmacopoeia. 1st ed. Ministry of Health, Republic of Indonesia, Jakarta. [Indonesian]

MoH RI. 2016. Proposal Guide, and Advanced Research Protocols: Research on Medicinal and Herbal Plants. Indonesian Center for Research and Development of Medicinal and Traditional Medicines, Tawangmangu, Karanganyar. [Indonesian]

Parekar RR, Dash KK, Marathe PA, Apte AA, Rege NN. 2012. Evaluation of Anti-inflammatory Activity of Root Bark of *Clerodendrum phlomidis* in Experimental Models of Inflammation. Intl J Appl Biol Pharmaceut Technol 3 (3): 54-60.

Pountos I, Georgouli T, Howard B, Giannoudis PV. 2011. Nonsteroidal anti-inflammatory drugs: prostaglandins, indications, and side effects. Intl J Interferon Cytokine Mediator Res 3: 19-27.

Prakash BN, Saravanan S, Pandikumar P, Bala KK, Karunai RM, Ignacimuthu S. 2014. Anti-inflammatory and anti-arthritic effects of 3-hydroxy, 2-methoxy sodium butanoate from the leaves of *Clerodendrum phlomidis* L.f. Inflam Res 63 (2): 127-138.

Prescott TAK, Kiapranis R, Maciver SK. 2012. Comparative ethnobotany and in-the-field antibacterial testing of medicinal plants used by the Bulu and inland Kaulong of Papua New Guinea. J Ethnopharmacol 139: 497-503.

Raja MKMM, Mishra SH. 2010. Comprehensive review of *Clerodendrum phlomidis*: a traditionally used bitter. J Chin Integrat Med 8 (6): 510-525.

Rathee P, Chaudhary H, Rathee S, Rathee D, Kumar V, Kohli K. 2009. Mechanism of Action of Flavonoids as Anti-inflammatory Agents: A Review. Inflam Allerg Drug Targets 8: 229-235

Ray SD, Ray S, Zia-Ul-Haq M, Feo VD, Dewanjee S. 2015. Pharmacological basis of the use of the root bark of *Zizyphus nummularia* Aubrev (Rhamnaceae) as anti-inflammatory agent. BMC Compl Altern Med 15: 416. DOI: 10.1186/s12906-015-0942-7.

RIMU [Research Institute of Mulawarman University]. 2015. Research on Local Ethnomedicine and Medicinal Knowledge Exploration in Indonesia: Community-Based in East and North Kalimantan. Agency for Health Research and Development, Ministry of Health [Research Report]. Agency for Health Research and Development, Ministry of Health, Jakarta. [Indonesian]

Siew CNG, Francis KLC. 2010. NSAID-induced Gastrointestinal and Cardiovascular Injury. Curr Opin Gastroenterol 26 (6): 611-617.

Souza TRCL, Marques GS, Vieira ACQM, Freitas JCR. 2012. State of the art of anti-inflammatory drugs. In: Badria F (ed). Pharmacotherapy. Intech, Rijeks, Croatia.

Sumi SA, Biswas NN, Islam MK, Ali MK. 2015. Evaluation of Analgesic and Antioxidant Properties in the Ethanolic Root Extract of *Clerodendrum viscosum* Vent. Intl J Pharm Sci Res 6 (5): 882-885.

Susiarti S, Purwanto Y, Windadri FI. 2009. Community knowledge of Pekurehua around Lore Lindu National Park, Central Sulawesi on medicinal plants and its utilization. Media Penelitian dan Pengembangan Kesehatan 19 (4): 185-192. [Indonesian]

Susiarti S, Rahayu M, Royyani MF. 2015. Knowledge and utilization of medicinal plants on Tobelo Dalam Community in North Maluku. Media Litbangkes. 25 (4): 211-218. [Indonesian]

Tasleem F, Azhar I, Ali SN, Perveen S, Mahmood ZA. 2014. Analgesic and anti-inflammatory activities of *Piper nigrum* L. Asian Pac J Trop Med 7 (Suppl 1): S461-S468.

Zhang J, Wang H, Wang T, Chong Y, Yu P, Lu C, Xue Y, Fu F, Zhang L. 2013. Anti-inflammatory activity of Yanshu spraying agent in animal models. Exp Therapeut Med 5: 73-76.

2_Anti-inflammatory_Activities_Swandari_Paramita.pdf

ORIGINALITY REPORT

7%	0%	7%	0%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	MK Nuryanto, S Paramita, A Iskandar. " Membrane stabilization activity as anti-inflammatory mechanisms of leaves extracts ", IOP Conference Series: Earth and Environmental Science, 2018 Publication	7%

Exclude quotes	Off	Exclude matches	< 3%
Exclude bibliography	On		