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Research Article

Anti-Inflammatory Activity of Ethanol And Fraction of Buni Leaves (*Antidesma Bunius L.*) on White Rat In Carrageenan Induced Paw Inflammation

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A B S T R A C T

Objectives: The purpose of this study was to investigate the anti-inflammatory effect ethanol extract and fraction of buni leaves (*Antidesma bunius L.)* in term of decreased edema volume of male white rat in 1% carrageenan-induced and also to determine the effective dose
Design: The design of this study was experimental, where the extraction and fraction of buni leaves were tested for inflammation inhibition value in carrageenan-induced white rats.The inflammatory activity test was divided 6 groups. The Group I (negative control) was given CMC 0.5%, Group II (positive control) was given diclofenac sodium 2,25 mg/kg bw (body weight), while Group III, IV, V and VI were given buni leaves extract and fraction at a dose of 100, 200 and 400 mg/kgbw respectively
Interventions: The variable that was intervened in this study was the concentration of extract used
Main outcome measure: The main measurement results in this study were to know the extracts and fractions which are capable inhibitor volume of edema in the carrageenan-induced rat paw
Results: the anti-inflammatory effects from buni leaves exhibited the most effective activity to reduce edema in the rat paw i.e. EEDB 200 mg / kg bw and FEADB 200 mg / kg bw showing the same value of against positive control
Conclusion: ethanol extract and ethyl acetate fraction buni leaves(*Antidesma bunius L.)* has an effective anti-inflammatory activity at a dose of 200 mg/kg bw.

Keywords: Anti-inflammation, Buni,Paw Edema, Carrageenan.

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INTRODUCTION

Inflammation is a normal protective body response caused by infectious agent factors, ischemia, antigen-antibody interactions, thermal or physical. As a result of these factors the body addresses responses such as the sensation of heat caused by increased movement of blood through dilated vessels into environmentally cooled extremities, also resulting in increased redness in the skin due to the additional number of erythrocytes in the area. Swelling (tumour) is the results of increased passage of fluid from dilated and permeable blood vessels into the tissues, infiltration of cells into the damaged area, in prolonged inflammatory responses deposition of connective tissue. Pain (dolor) is due to the direct effects of mediators, either from initial damage or that resulting from the inflammatory response and the stretching of sensory nerves due to edema. The loss of function refers to either simple loss of mobility in a joint, due to the edema and pain, or to the replacement of functional cells-[1-2].

Inflammatory treatment that is often used i.e. steroidal anti-inflammatory drug (SAID) and nonsteroidal anti-inflammatory drug (NSAID), the drug is usually used to eliminate inflammatory diseases, but the drug has side effects such as bleeding gastrointestinal and peptic ulcer [3]. Therefore, it need to found alternative drug from to avoid adverse event from conventional treatment i.e. herbal medicine from plant.

One of the plants that have the potential to be developed is the Antidesma bunius (L.) buni plant. Plants that grow wild in wet areas and can be found in the lowlands of India, Sri Lanka, Burma, Malaysia, Indonesia, New Guinea and Australia[4].Several previous studies showed that the ethanol extract of buni leaves contained flavonoids, tannins, saponins and phenols in their leaves.[5-6]. Flavonoids work to inhibit an important phase in prostaglandin biosynthesis, inhibit leukocyte accumulation in the injured area, inhibit the degradation of neutrophils and inhibit histamine release so they can become anti-inflammatory [7].

Based on the description above this study aims to assess the anti-inflammatory activity of ethanol and fraction of buni leaves (antidesma bunius l.) On white rat in carrageenan-induced paw inflammation.

MATERIAL AND METHODS

Plant and Chemical Material

Buni leaves sample were collected from Medan, Northern Sumatera, Indonesia. The part of the plant used is leaves. Buni leaves have been determined by the Herbarium Bogoriense Indonesian Institute of Science is known that the species is *Antidesma bunius* L. with Family Phyllanthe ceae.

Extraction and fraction of Buni

The dried Buni leaves (1000 g) were crushed using blender. Afterwards, the leaves powders were submerged with ethanol 80% for 5 days, then were resubmerged for 2 days. The solvent was evaporated at low pressure and temperature not exceeds 60^0 C using rotary evaporator, then dried using freeze dryer. Next, the crude extract was taken (90 g) for liquid-liquid extraction to obtain a nonpolar (using n-hexane), semipolar (using ethyl acetate) and polar fraction [8].

Experimental Animals

Male wistar rat (150-200g) were used in the entire study. The animals were fed with standard laboratory diet and water ad libitum. The experimental protocol was approved by the Institutional Animal Ethics Committee.

Distribution of test animals

Tests were given orally to each of the 6 male wister rats in each group. In this test there were 6 groups consisting of 2 control groups and 4 test groups consisting of a dose of 100 mg / kg, 200 mg / kg, 400 mg / kg, summarized as follows:

Table 1: Distribution of test groups

No	Group name	Group
I	CMC Sodium	Negative control, suspension CMC Sodium 0,5%
II	Diclofenac Sodium	Positive control, suspension diclofenac sodium dosage 2,25 mg/kg
III	EEDB	Test group, suspension of buni leaves ethanol extract dosage 100mg/kg, 200mg/kg, 400mg/kg
IV	FNHDB	Test group, suspension N-hexane fraction of buni leaves dosage 100mg/kg, 200mg/kg, 400mg/kg
V	FEADB	Test group, suspension ethyl acetate fraction of buni leaves dosage 100mg/kg, 200mg/kg, 400mg/kg
VI	SDB	Test group, suspension residual fraction of buni leaves dosage 100mg/kg, 200mg/kg, 400mg/kg

Anti-inflammatory test

Each group of test animals is given preparations via oral. Marked on rat paw as the measurement limit on the plethysmometer, measure normal paw volume at 30 minutes after administration of 0.05ml of carrageenan solution in each test animal with a concentration of 1% on the sole of the paw. Furthermore, the volume of rat paw was measured at 1, 2, 3, 4, 5 and 6 hours after carrageenan was induced. Based on the measurement results obtained udema value data by reducing the volume of udema formed at each time measurement of normal paw volume and percent inhibition of udema by calculating the percentage of udema ratio formed at each measurement time.

The formula for measuring udema values and percent inhibition of udema is as follows [9]:

$$\% R = \frac{Vt - Vo}{Vo} x\ 100\%$$

%R = percentage of inflammation
Vo = initial paw volume
Vt = volume of edema paw at time T

The percentage of inflammatory inhibition (%IR) can be calculated using the following formula [9].

$$\%IR = \frac{a - b}{A} \text{ x } 100\%$$

% IR = Percentage of inflammation inhibition
a = Percentage of inflammation in the average control treatment group
b = Percentage of inflammation of the average test group

RESULT AND DISCUSSION

Extraction and Fractionation

The extract was obtained by extraction process by maceration of 1000g of buni leaves simplicia powder obtained 200g of buni leaves ethanol extract, then fractionation of 80g ethanol extract using a separating funnel to obtain 300mg n-hexane fraction, ethylacetate fraction 2g and fraction remaining 5g.

Anti-inflammatory test

The test of anti-inflammatory effects is carried out using a digital pletismometer with the principle of measurement based on Archimedes' law that is objects that are inserted into the liquid will exert a force or pressure up to the amount of the displaced volume. This digital pletismometer method was chosen because it has advantages in terms of fast in implementation, observations of measured rat paw volume are more accurate, because the measured rat paw volume is recorded on a digital recorder, the sensitivity of the tool is higher than mercury pletismometer[10]. Data obtained were analyzed by analysis of variance (ANOVA) using the SPSS 20 program.

Paw edema caused by carrageenan induction. Carrageenan is a linear polymer composed of about 25,000 galactose

derivatives whose structure depends on the source and extraction conditions. Carrageenan is grouped into 3 groups of groups of kappa, iota, and lambda carrageenan (λ carrageenan) is carrageenan which is isolated from the *Gigartinapistillata* or *Chondruscrispus* algae, which can dissolve in cold water. Carrageenan was chosen to test anti-inflammatory drugs because they are not antigenic and do not cause systemic effects [10-11].

Anti-inflammatory measurements were carried out by looking at the ability of buni leaves to reduce the swelling of the legs of experimental animals due to injection of 1% carrageenan solution. After being injected with carrageenan, the mice showed swelling and redness in the legs and the mice could not walk as agile as before the injection. The principle in this method measures the volume of swollen soles of the feet of test animals that have been induced by an inflammatory agent [11]. The results of this study are reflected in percent inflammation and percent inflammation inhibition. The percentage of inflammation produced in this study can be shown in figure 1.

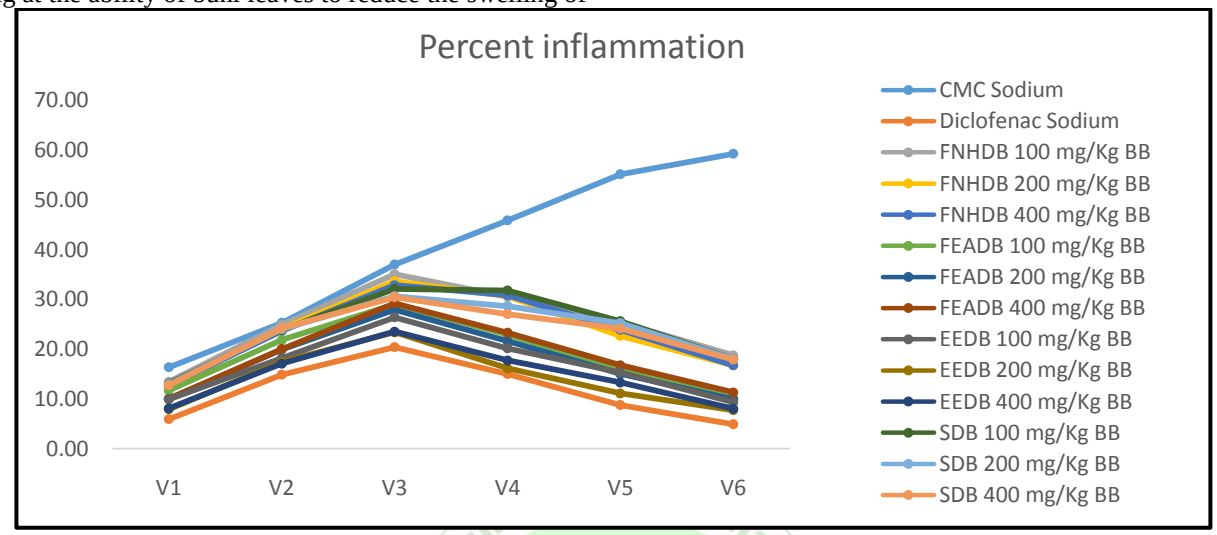

Figure 1: Effect of treatment on average percent inflammation

Based on the average results of percent inflammation obtained then the percent value of udema inhibition was calculated which illustrates the ability of the test sample to resist inflammation that occurs due to carrageenan induction. The results of calculating inflammation inhibition percent can be seen in Figure 2.

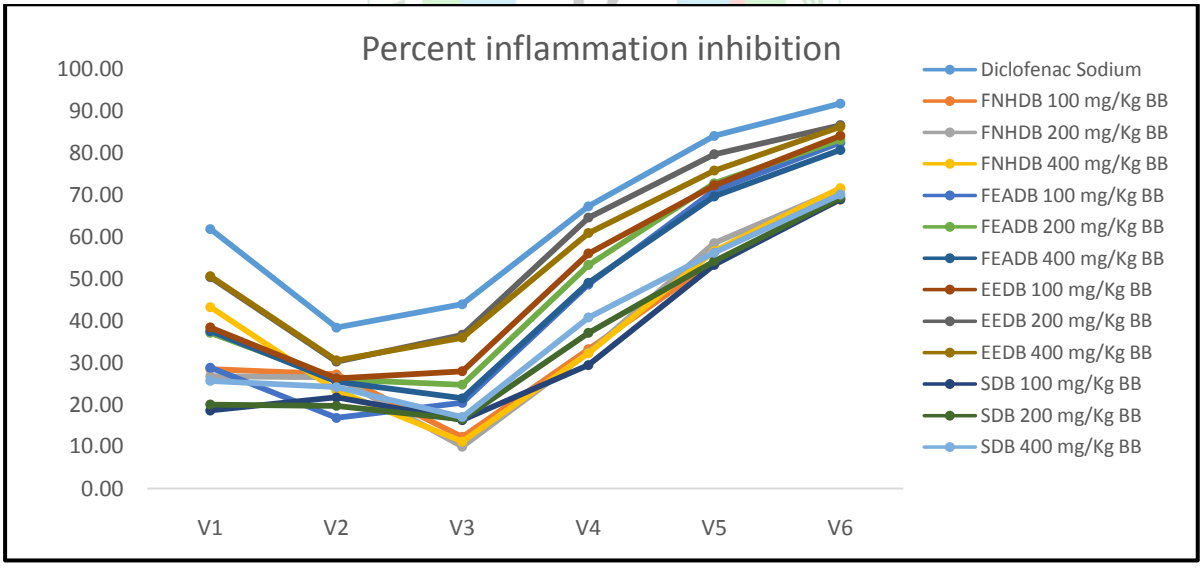

Figure 2: Effect of treatment on percent inflammation inhibition

The negative control group that was given 0.5% CMC suspension without any active compounds in it, it was seen a very significant increase in paw volume with a much larger volume than the other test groups. This negative group becomes a reference in comparing the results achieved by other groups. The test group with results that differed significantly from the negative control group showed the effect of the compounds or medicinal ingredients given to the test animals.

The positive control group was given suspension of diclofenac sodium at a given dose of 2.25 mg / kg. The results obtained by this group differed significantly from the negative controls in each measurement time, namely at the 1st, 2nd, 3rd, 4th, 5th and 6th hours. The results of the positive group were compared with the test group given ethanol extract, fraction n-hexane and ethyl acetate fraction in buni leaves in doses of 100 mg / kg, 200 mg / kg and 400 mg / kg body weight have different results.

Based on the results of the average percent inflammation of the rats, that there was an increase in percent inflammation in the 1st to 3rd hours after being given treatment, then there was a decrease in the 4th to 6th hours in the EEDB group 100 mg / kg bw (body weight), EEDB 200 mg / kg bw, EEDB 400 mg / kg bw, FEADB 100 mg / kg bw, FEADB

200 mg/kg bw, FEADB 400 mg/kgbw. While in the FNHDB group 100mg/kgbw, FNHDB 200 mg/kgbw FNHDB 400 mg / kg bw, SDB 100 mg / kg bw, SDB 200mg/kg bw, and SDB 400mg/kgbw there was an increase in percent inflammation in the 1st to 3rd hours after being given treatment, then there was a decrease in the 4th to 6th hours after being treated, but not as big as the EEDB group and FEADB group.

The negative CMC control a 0.5% percent increase in inflammation occurs up to the 6th hour while in positive control sodium diclofenac increases the percentage of inflammation occurring at the 1st to 3rd hour after being treated, then a decrease in the 4th hour to the hour 6th.

Furthermore, the percentage of inflammation data of each rat in all groups was calculated by paw test, then the statistics were analyzed using the SPSS 20 program. The results of the SPSS program can be seen as the significance values in table 1.

Table 2: Results of the effect of treatment on the average percentage of inflammation

No	Group	The average percentage of inflammation (hour)					
		1	2	3	4	5	6
1	Negative Control	16,34 ± 2,32 #	25,27 ± 5,52 #	36,96 ± 4,88 #	45,87 ± 5,80 #	55,12 ± 3,54 #	59,23 ± 6,46 #
2	Positive Control	5,96 ± 2,26 *	14,87 ± 4,74 *	20,39 ± 5,89 *	14,97 ± 3,20 *	8,78 ± 2,16 *	4,91 ± 1,87 *
3	EEDB 100 mg/kg bw	9,93 ± 3,06 *	18,26 ± 2,20	26,39 ± 1,69 *	20,14 ± 2,28 *	15,31 ± 2,60 #	9,36 ± 3,40 *
4	EEDB 200 mg/kg bw	7,96 ± 1,85 *	17,40 2,97	23,38 ± 3,29 *	16,12 ± 4,62 *	11,12 ± 2,43 *	7,75 ± 2,03 *
5	EEDB 400 mg/kg bw	8,10 ± 2,22 *	17,07 ± 3,49	23,51 ± 4,96 *	17,73 ± 5,53 *	13,30 ± 5,09 *	8,04 ± 2,22 *
6	FNHDB 100 mg/kg bw	13,43 ± 3,86 #	24,85 ± 6,06 #	35,05 ± 7,85 #	30,58 ± 7,91 *#	25,41 ± 9,13 *#	18,75 ± 6,60 *#
7	FNHDB 200 mg/kg bw	12,38 ± 2,53 #	24,07 ± 4,95 #	33,66 ± 6,41 #	30,61 ± 3,46 *#	22,63 ± 4,34 *#	16,76 ± 3,15 *#
8	FNHDB 400 mg/kg bw	12,70 ± 5,98 #	23,64 ± 5,01 #	32,84 ± 5,18 #	30,79 ± 4,37 *#	23,87 ± 2,10 *#	16,75 ± 2,80 *#
9	FEADB 100 mg/kg bw	11,70 ± 2,96	21,84 ± 3,36	29,00 ± 4,37	22,87 ± 4,92 *	15,83 ± 3,21 *	10,15 ± 3,02 *
10	FEADB 200 mg/kg bw	10,03 ± 1,96 *	19,97 ± 3,88	27,94 ± 5,58	21,60 ± 4,52 *	15,04 ± 3,21 *	9,89 ± 3,64 *
11	FEADB 400 mg/kg bw	10,02 ± 2,83 *	20,01 ± 3,55	29,22 ± 4,46	23,29 ± 3,94 *	16,78 ± 3,44 *	11,29 ± 3,59 *
12	FSDB 100 mg/kg bw	13,10 ± 1,94 #	23,84 ± 4,53 #	32,12 ± 6,34 #	31,82 ± 6,77 *#	25,25 ± 2,85 *#	18,01 ± 6,65
13	FSDB 200 mg/kg bw	12,96 ± 1,76 #	24,01 ± 2,89 #	30,62 ± 2,47 #	28,66 ± 3,24 *#	25,25 ± 2,85 *#	18,04 ± 2,33
14	FSDB 400 mg/kg bw	12,75 ± 3,13 #	24,17 ± 2,90 #	30,43 ± 4,40	27,00 ±2,85 #	24,14 ± 5,00 *#	17,88 ± 6,06

Keterangan : *p<0,05 (significantly different from negative control CMC 0,5%)
#p>0, 05 (significantly different from positive control diclofenac sodium2, 25 mg/kg).

Based on these results it can be concluded that FNHDB at a dose of 200 mg / kg bw, FNHDB 400 mg / kg bw, FSDB 400 mg / kg bw, FSDB 200mg / kgbw, FNHDB 100 mg / kg and FSDB 100 mg / kg bw have activity anti-inflammatory but not potential in suppressing edema that occurs in the legs of test animals, shown from the measurement results that differ significantly from the positive control.

The group EEDB 200 mg / kg bw, EEDB 400 mg / kg bw, EEDB 100 mg / kg bw, FEADB 400 mg / kg bw, FEADB 200 mg / kg bw, and FEADB 100 mg / kg bw showed significant differences in negative control and vice versa does not show any significant difference in positive control. Among all groups of EEDB dose test 200 mg / kg bw had the most potent anti-inflammatory activity in suppressing edema that occurred in the legs of test animals, indicated by the results of measurements similar to sodium diclofenac 2.25 mg / kg as a positive control. Whereas among the fraction groups that have the most potent anti-inflammatory activity in suppressing edema, namely FEADB 200 mg / kg bw.

Based on the results of the calculation of the percentage of edema inhibition and after statistical tests, the same results were obtained for the edema value that occurred. Percentage of inhibition of diclofenac sodium 2.25 mg / kg as a positive control as a standard reference in looking at the potential of drug compounds in suppressing inflammation that will occur after carrageenan-induced test animals, the results of statistical tests can be seen in table 2.

Table 3: Results of treatment effects on inflammation inhibition rates

No	Group	Average percent inflammation (hour)					
		1	2	3	4	5	6
1	Positive Control	61,83 ± 17,79 *	38,30 ± 23,02 *	43,91 ± 18,20 *	67,24 ± 5,98 *	83,97 ± 4,11 *	91,70 ± 3,24 *
2	EEDB 100 mg/kg bw	38,35 ± 20,04	26,22 ± 9,13 *	27,92 ± 7,01	55,95 ± 2,92 *	72,23 ± 4,37 *	84,03 ± 3,40 *
3	EEDB 200 mg/kg bw	50,35 ± 13,64	30,18 ± 8,05 *	36,60 ± 5,86 *	64,52 ± 11,04 *	79,63 ± 5,27 *	86,54 ± 4,48 *
4	EEDB 400 mg/kg bw	50,52 ± 10,63	30,51 ± 16,00 *	35,92 ± 13,17*	60,82 ± 13,49 *	75,74 ± 9,86 *	86,14 ± 4,61 *
5	FNHDB 100 mg/kg bw	28,41 ± 15,44 #	27,17 ± 16,11 *	12,26 ± 7,31 #	33,17 ± 17,10 #	54,08 ± 16,20 #	68,81 ± 9,06 #
6	FNHDB 200 mg/kg bw	26,72 ± 15,44 #	26,44 ± 13,96 *	9,93 ± 10,20 #	32,33 ± 11,92 #	58,43 ± 10,32 #	71,26 ± 7,10 #
7	FNHDB 400 mg/kg bw	43,14 ± 20,58	23,25 ± 12,65 *	11,15 ± 9,67 #	32,18 ± 11,37 #	56,56 ± 4,22 #	71,55 ± 4,96 #
8	FEADB 100 mg/kg bw	28,79 ± 18,04	16,82 ± 7,41 *	20,42 ± 14,99 #	48,58 ± 16,02	70,92 ± 7,42 *	82,38 ± 6,58
9	FEADB 200 mg/kg bw	37,04 ± 17,18	25,99 ± 13,47 *	24,69 ± 8,53	53,21 ± 5,66 *	72,72 ± 5,51 *	83,07 ± 6,44 *
10	FEADB 400 mg/kg bw	37,45 ± 19,94	25,42 ± 12,00 *	21,47 ± 12,72	48,95 ± 8,65	69,59 ± 5,71	80,62 ± 6,53
11	FSDB 100 mg/kg bw	18,55 ± 14,94 #	21,71 ± 8,30 *	16,27 ± 12,33 #	29,41 ± 18,90 #	53,25 ± 11,66 #	68,87 ± 13,71 #
12	FSDB 200 mg/kg bw	19,95 ± 11,43 #	19,70 ± 16,54 *	16,47 ± 8,07 #	37,06 ± 7,80 #	54,14 ± 4,77 #	69,23 ± 5,05 #
13	FSDB 400 mg/kg bw	25,63 ± 19,77 #	24,13 ± 17,12 *	17,00 ± 12,26 #	40,70 ± 6,97 #	56,17 ± 8,46 #	70,03 ± 8,90 #

Keterangan : *p<0,05 (significantly different from negative control CMC 0,5%)
#p>0,05 (significantly different from positive control Diclofenac Sodium 2,25 mg/kg).

The results of statistical tests showed that the FNHDB group was 100 mg / kg bw, FNHDB 200 mg / kg bw, FNHDB 400 mg / kg bw, FSDB 100 mg / kg bw, FSDB 200 mg / kg bw, and FSDB 400 mg / kg bw, shows the activity of suppressing edema that occurs, but it is less able to approach the value of sodium diclofenac 2.25 mg / kg on each

measurement. EEDB group 200 mg / kg bw showed good results, where this group was able to approach the value of diclofenac sodium 2.25 mg / kg based on statistical tests stating that the results of this group were not significantly different from positive controls.

The anti-inflammatory effect is thought to be due to the activity of secondary metabolites found in buni leaves, namely flavonoids[13], steroids/triterpenoids, glycosides, and saponins[4-6]. This is supported by the results of phytochemical screening tests that show the presence of these groups of compounds.

The mechanism of flavonoids as an anti-inflammatory can be through several paths:

1. Inhibition of COX and/or lipoxygenase enzyme activity, due to inhibition of COX or lipoxygenase. This inhibition of the COX and lipoxygenase pathways also causes inhibition of the biosynthesis of eicosanoids and leukotrienes, which are the final products of the COX pathway and lipoxygenase [7,12,13,14,15].
2. Inhibition of leukocyte accumulation, where the anti-inflammatory effect of flavonoids can be caused by its action to inhibit leukocyte accumulation in the inflammatory area. normal conditions leukocytes move freely along the endothelial wall. During inflammation, various endothelial derivative mediators and complement factors may cause leukocyte adhesion to the endothelial wall so that leukocytes become immobilized and stimulate neutrophil degranulation, mentioning that administration of flavonoids can reduce immobilized leukocyte count and reduce complement activation thereby reducing leukocyte adhesion to endothelium and resulting a decrease in the body's inflammatory response[7,12,13,14,15].
3. Inhibition of histamine release. The anti-inflammatory effect of flavonoids is supported by its action as an anti-histamine. Histamine is an inflammatory mediator whose release is stimulated by pumping calcium into cells[14-15]. The Nijveldt et al., (2001) study reported that flavonoids can inhibit histamine release from mast cells (7). The exact mechanism is unknown, but suspect that flavonoids can inhibit the c-AMP phosphodiesterase enzyme so that the levels of c-AMP in mast cells increase, so calcium is prevented from entering the cell which means it also prevents histamine release[16].

CONCLUSIONS

The extract buni leaves at a dose of 200 mg / kg bw at the 4th to 6th hours has an effective anti-inflammatory activity against reducing the volume of edema in the rat paw induced with carrageenan, but in the fraction that has anti-inflammatory effectiveness is a dose of 200 ethyl acetate mg / kg bw.

REFERENCES

1. Punchard NA, Whelan CJ, Adcock I. The Journal of Inflammation. J Inflamm. 2004; 1(1):1–4.
   Stankov S V. Definition of Inflammation, Causes of Inflammation and Possible Anti-inflammatory Strategies. Open Inflamm J. 2012; 5(1):1–9.
2. Amri O, Zekhnini A, Bouhaimi A, Tahrouch S, Hatimi A. Anti-inflammatory Activity of Methanolic Extract from Pistacia atlantica Desf. Leaves. Pharmacogn J. 2018; 10(1):71–6.
3. Kassem M, Hashim A, Hassanein H. Bioactivity of Antidesma bunius leaves (Euphorbiaceae) and their major phenolic constituents. Eur Sci J. 2013; 9(18):217–28.
4. Pongnaratorn P, Kuacharan P, Kotsuno V, Pakdee N, Sriraj P, Sattayasai J. In vitro antimicrobial activity of Antidesma bunius extracts on oral pathogenic bacteria. Thai J Pharm Sci. 2017; 41(4):144–9.
5. Tawali S, Asad S, Hatta M, Bukhari A, Khairi N, Rifai Y, et al. Anthocyanin-rich Buni-berry (Antidesma bunius) Extract Increases Paraoxonase 1 Gene Expression in BALB/c Mice Fed with a High-fat Diet. J Young Pharm. 2019; 11(1):46–50.
6. Nijveldt R j, Nood E Van, Hoom DE, Boelens PG, Norren K van, Leeuwen PA. Flavonoids : a review of probable mechanisms of action and. 2001; 74(4):18–24.
7. Nn A. A Review on the Extraction Methods Use in Medicinal Plants, Principle, Strength and Limitation. Med Aromat Plants. 2015; 04(03):3–8.
8. Yu D, Yuan Y, Jiang L, Tai Y, Yang X, Hu F, et al. Anti-inflammatory effects of essential oil in Echinacea purpurea L. Pak J Pharm Sci. 2013; 26(2):403–8.
9. Fehrenbacher JC, Vasko MR, Duarte DB. Models of Inflammation: Carrageenan- or CFA-Induced Edema and Hypersensitivity in the Rat. Curr Protoc Pharmacol. 2018;
10. Lalan BK, Hiray RS, Ghongane BB. Evaluation of analgesic and anti-inflammatory activity of extract of Holoptelea integrifolia and Argyreia speciosa in animal models. J Clin Diagnostic Res. 2015; 9(7):1–4.
11. Cruz MP, Andrade CMF, Silva KO, De Souza EP, Yatsuda R, Marques LM, et al. Antinoceptive and anti-inflammatory activities of the ethanolic extract, fractions and flavones isolated from mimosa tenuiflora (Willd.) Poir (Leguminosae). PLoS One. 2016; 11(3):1–29.
12. Panche AN, Diwan AD, Chandra SR. Flavonoids: an overview. J Nutr Sci. 2016; 5.
13. Pérez-Cano FJ, Castell M. Flavonoids, inflammation and immune system. Nutrients. 2016; 8(10):8–11.
14. Kumar S, Pandey AK. Chemistry and Biological Activities of Flavonoids: An Overview. Sci World J. 2013; 2013.
15. Mueller F-J, McKercher SR, Imitola J, Loring JF, Yip S, Khoury SJ, et al. At the Interface of the Immune System and the Nervous System: How Neuroinflammation Modulates the Fate of Neural Progenitors In Vivo. In: Opportunities and Challenges of the Therapies Targeting CNS Regeneration. 2006.