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ANTI-INFLAMMATORY ACTIVITIES OF AQUEOUS EXTRACT OF BERINGIN (*FICUS BENJAMINA* L.) AND KERSEN (*MUNTINGIA CALABURA* L.) LEAVES IN ALBINO RATS

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ABSTRACT

Inflammation can increase the risk of various diseases. Currently, many drugs to treat inflammation have serious side effects. Ficus benjamina L. and Muntingia calabura L. have the potential to be safer and more efficient anti-inflammatory agents. Many pharmacological studies of the leaves of these plants have been carried out, but mostly did not use water extract even though traditionally the leaves were taken as infusion or decoction. This research aimed to prove the anti-inflammatory activities of aqueous extract of Ficus Benjamina L. and Muntingia Calabura L. leaves scientifically. Extraction was conducted by the Dekok method. Anti-inflammatory activities were performed based on the inhibition of edema on the paw of the rats, induced by carrageenan lambda 1 % intraplantarely. Results showed that all of the doses of the aqueous extract of Ficus benjamina L. and Muntingia calabura L. leaves had anti-inflammatory activities compared to the negative control ($p<0.05$). The highest anti-inflammatory activity on the aqueous extract of Ficus benjamina L. leaves was shown at the dose of 264 mg/kg bw with the edema volume percentage 39.71% compared to negative control group 70.12% and percentage of inflammation inhibition was 44.36%. On the aqueous extract of Muntingia calabura L. leaves, the highest anti-inflammatory activity was shown at the dose of 1284 mg/kg bw with the edema volume percentage 38.90%, and the percentage of inflammation inhibition was 46.83%.

INTRODUCTION

Inflammation is a physiological process that involves the intervention of the immune system (Bouyahya et al., 2021). The common physiological outcomes of inflammation are characterized by pain, redness, swelling, heat and loss of tissue function (Chen et al., 2018). Although inflammation is needed for protection, however, the prolonged response of the immune system can increase the risk of various diseases like Alzheimer's disease, rheumatoid arthritis, diabetes, cancer, and several other neurological diseases (Xue et al., 2019).

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There are currently many synthetic drugs on the market to treat inflammation-related diseases, but the side effects caused by these drugs are quite serious and less potent (Xue et al., 2019). The NSAIDs such as aspirin, ibuprofen and diclofenac (Lu et al., 2022) are the most commonly prescribed drugs for treating inflammation globally that have multiple side effects and allergic reactions like gastrointestinal disorders, renal disorder, cardiovascular disease, hepatotoxicity, and hypertension (Bindu et al., 2020). Considering these side effects, it is deemed necessary to develop safer and efficient anti-inflammatory drugs especially from traditional medicines which have been known for their efficacy (Derouich et al., 2020).

The various activities of medicinal plants are caused by the content of secondary metabolites such as flavonoid, phenolics, alkaloids, saponins, steroids, terpenoid, tannins (Verawati et al., 2017) and also polysaccharide, phenylpropanoid, lignanoid, coumarin, and anthraquinone that have been reported to have the anti-inflammatory activities both in *vitro* and in *vivo* (Hou et al., 2020).

In Indonesia, many people use the plants as traditional medicine for generations, which is proven by the existence of old manuscripts on the palm (lontar) leaves of Husodo (Java), Usada (bali), lontarak pabbura (South Sulawesi) and reliefs from Borobudur temple that depicting people mixing medicine using plants as the raw material (Sari, 2006). Although Indonesia has quite a large of biodiversity, that is around 35,000 of potential medicinal plants, but its use as traditional medicine is still relatively low, only about 3500 species of medicinal plants (Badrunasar & Santoso, 2016).

Some plants that have been empirically used by the community to treat problem in health including inflammation are beringin (*Ficus benjamina* L.) and kersen (*Muntingia calabura* L). The leaves, bark and fruits of beringin (*Ficus benjamina* L.) contain cinnamic acid, lactose, naringenin, quercetin, caffeic acid and stigmasterol (Imran et al., 2014); (Ashraf et al., 2020) and have been used in Indonesia traditionally for anti-influenza, malaria, bronchitis, pertussis, dysentery, and hot seizures in children (Hasti et al., 2014). Several studies also proved that *ficus benjamina* leaves have pharmacological activities such as antiviral agent against *Herpes simplex* virus 1 and 2 (Yarmolinsky et al., 2012), antioxidant (Jain et al., 2014), antibacterial and antihemolytic (Singh jassal & Sharma, 2019).

The leaves of kersen (*Muntingia calabura* L.) contain tocopherol, many various flavonoids like flavone, flavanones, chalcones, coumarate, stigmasterol, vanillic acid and polyphenol (proanthocyanidin and cyanidin) (Mastuki et al., 2019). *Muntingia calabura* L. traditionally has been used to reduce prostate gland swelling, gastric ulcer, cold, headache and infections in general (Seixas et al., 2021). Its pharmacological activities also had been proven by research as antipyretic, anti-ulcer (Mastuki et al., 2019), antioxidant, antidiabetic, analgesic, antibacterial and nephroprotective (Fitrianda et al., 2019). The anti-inflammatory activity had been reported by previous studies using methanol extract (Jisha et al., 2019) and chloroform extract (Mastuki et al., 2019) of *muntingia calabura* L. leaves.

According to all the previous researches related to the pharmacological activities of *Ficus benjamina* L. and *Muntingia calabura* L. that have been mentioned above, mostly they used either methanol, ethanol or chloroform extract of the leaf, whereas for aqueous extract was rarely used even though traditionally the leaves were taken as infusion or decoction using boiled water (Mastuki et al., 2019). Therefore, this study aimed to prove the anti-inflammatory activities and to determine the effective dose of the water extract of beringin (*Ficus benjamin*a L.) and Kersen (*Muntingia calabura* L.) leaves scientifically.

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RESEARCH METHODE

Plant Material

Beringin (*Ficus benjamina* L.) and Kersen (*Muntingia calabura* L.) leaves were collected from various parts of Kupang city, East Nusa Tenggara. The plants material was identified and authenticated taxonomically at Herbarium Bandungense, School of Life Sciences and Technology, Bandung Institute of Technology.

Preparation of Extract

Beringin (*Ficus benjamina* L.) and Kersen (*Muntingia calabura* L.) leaves were extracted by dekok methode. As much as 200 grams of plants dried leaves were boiled with distilled water at 90 ^{O}C of temperature for 30 minutes. The aqueous extract was filtered and evaporated in a carefully regulated water bath maintained at a temperature of 50 ^{O}C.

Experimental Animal

Male *wistar* rats with a weight of 180-210 grams. The experimental animals were adapted for one week before the experiment was carried out. Animal's body weight was weighed every day and only healthy and normal animals were used for experiment. The animals were deprived of food for 18h before the test.

Anti-inflammatory activity

Anti-inflammatory activities were performed base on the inhibition of edema formation on the paw of the rats induced by 0.05 mL of carrageenan lambda 1 % injected intraplantarely. This method is one of the most commonly employed methods for the screening of acute inflammation (Mittal et al., 2017). Experimental rats were divided into 6 groups that each group contains 5 rats. All groups were given tested aqueous extracts and selected standard drug one hour before the carrageenan challenge with the settings namely in the negative control group received only Gom Arab 2% suspension and in the positive control group received 4,5 mg/kg bw of diclofenac sodium. Rats in the rest of the groups received respectively aqueous extracts of *Ficus benjamina* L. leaves in doses of 264 and 528 mg/kg bw and also the aqueous extract of *Muntingia calabura* L. leaves in doses of 642 and 1284 mg/kg bw. The edema formation was measured volumetrically with plethysmometer every 15 minutes for 3 hours. Collected data were analyzed statistically using one way Anova.

Edema volume and Inhibition of inflammation percentages were calculated using the following formula (Mittal et al., 2017) :

$$\% \text{ Edema Volume} = \frac{\text{Edema after induction} - \text{Edema before induction}}{\text{Edema volume before induction}} \times 100$$

$$\% \text{ Inflammation Inhibiton} = \frac{\text{Mean Edema control} - \text{Mean Edema Drug Treated}}{\text{Mean Edema Control}} \times 100$$

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RESULT AND DISCUSSION

The anti-inflammatory activity of each test group was shown by the smaller percentage of the volume of edema formed and the greater percentage of inflammation inhibition. As seen on the graphic, the greatest anti-inflammatory activity was shown by the positive control group (diclofenac sodium 4.5 mg/kg bw) with edema volume percentage of 25.58% and the inflammation inhibition percentage of 53.18%. Fairly good anti-inflammatory activities although had significant different ($p< 0.05$) with positive control group, were also shown by the aqueous extract group of beringin (*Ficus benjamina* L.) leaves doses of 264 and 528 mg / kg bw and aqueous extract of kersen (*Muntingia calabura* L.) leaves at doses of 642 and 1284 mg / kg bw with the edema volume percentage, respectively 39.71%, 42.42%, 40.8 % and 38.90% and also the inflammation inhibition percentage respectively 44.36%, 43.67%, 43.59% and 46.8 % (figure 1).

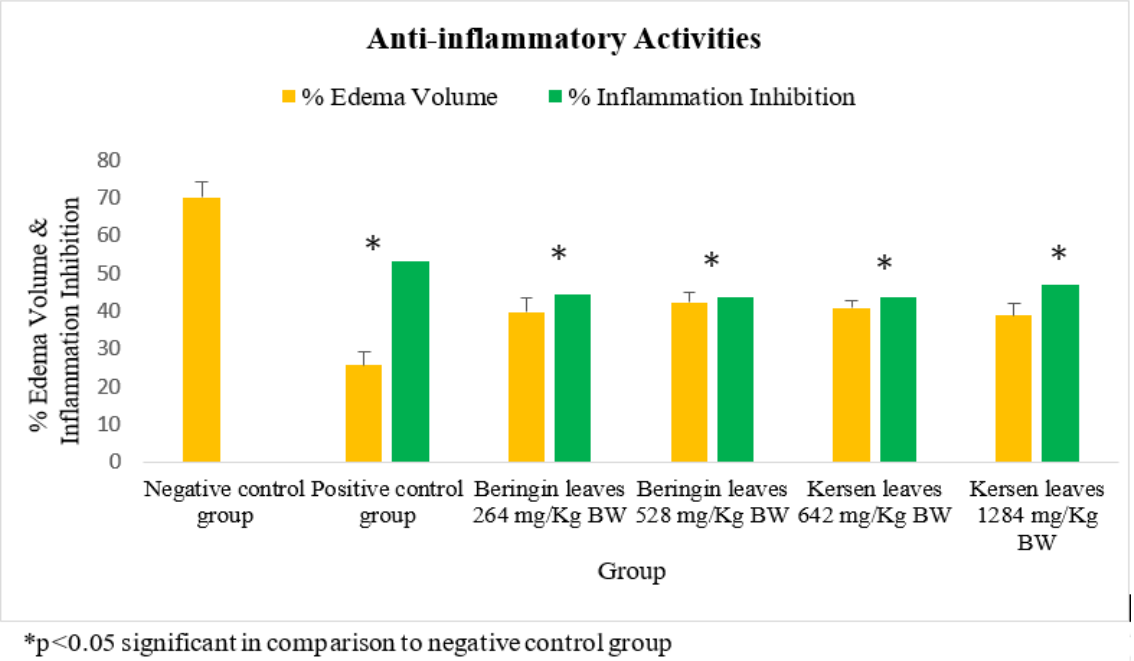

Figure 1, Percentage of Edema Volume and Inflammation Inhibition

All doses of aqueous extract group and positive control group had significantly different ($p<0.05$) of anti-inflammatory activities compared to the negative control group, which had the percentage of edema volume of 70.12% and had no resistance to inflammation. Statistically, between all doses of aqueous extract of beringin and kersen, did not have a significant difference but the biggest anti-inflammatory activities among them which approaching to the anti-inflammatory activity shown by positive control group, were shown by the aqueous extract of beringin leaves with a dose of 264 mg / kg bw and the aqueous extract of kersen leaves at dose of 1284 mg / kg bw.

The ability of aqueous extracts of *Ficus benjamina* L. and *Muntingia calabura* L. leaves to suppress inflammation is thought to be inseparable from the presence of several

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phytochemical components on the aqueous extracts, especially the presence of various flavonoids (Ginwala et al., 2019). Aqueous extracts of *Ficus benjamina* L. and *Muntingia calabura* L. leaves are thought surpress inflammation in all phases, its because of the used of carrageenan on the research to induce edema in the paw of the rats. Carrageenan provides a model of acute inflammation, in which several inflammatory mediators are involved. In the initial phase, around the first 1.5 hours, histamine and seretonin are released, then in the second phase, about 1.5 to 2.5 hours, bradykinin is involved. In the third phase, about 2.5 to 6 hours after carrageenan induction, the inflammatory process is mediated by prostaglandins (Mittal et al., 2017). According to that also, it could be suggested that the possible mechanism of the anti-inflammatory action of *Ficus benjamina* L. and *Muntingia calabura* L. leaves could be due to inhibition of release of mediators in all phases.

CONCLUSION

Base on the present study it could be concluded that aqueous extract of Beringin (*Ficus benjamina* L.) and Kersen (*Muntingia calabura* L.) leaves might be helpful in preventing inflammatory. The Data showed that all of doses of the aqueous extract groups had anti-inflammatory activities which was significantly different with negative control ($p<0.05$). However, the detailed mechanism of these extracts in inhibiting inflammation still needs further investigation

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