TEST OF ANTI-INFLAMMATION ACTIVITIES OF
PEPAYA LEAF (Carica papaya L.) EXTRACT ON MALE
WISTAR RATS INDUCED BY CARAGENAN 1%

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Abstract. Inflammation is a normal protective response to tissue injuries caused by physical trauma, destructive chemicals, or microbiological substances. The purpose of this study was to determine the anti-inflammatory activity of papaya leaf water extract (Carica papaya L.) on the feet of male Wistar rats which were induced by carrageenan 1%. The research method used is experimental. The stages of this study include plant identification, making dry simplicia powder, simplicia characteristics, extracting papaya leaves using water, simplicia phytochemical screening and papaya leaf water extract (EADP), as well as testing for anti-inflammatory activity. Anti-inflammatory testing was carried out on 20 male Wistar rats induced with 1% carrageenan sub plantar. The test group was divided into five groups for the induction, comparison, EADP 50, 100, 200 mg/kg BW groups. The parameters observed were the volume of mouse leg edema measured by a plethysmometer every 30 min for 5 h. Data obtained then calculated percent inflammation and percent inflammation inhibition. Furthermore, it was analysed by ANOVA with a confidence level of 95%. The results of the simplicia characteristics showed that the water content, water content of the sea water and soluble extracts of ethanol were 8.9%, 51.4% and 10.2% respectively. The results of simplicia and EADP phytochemical screening showed the content of flavonoids, tannins, triterpenoids, glycosides, and alkaloids. Observations of the percentage of inflammation in the induction group had the highest percentage of inflammation compared with the other test groups at time of 300 min (p < 0.05). Whereas the percentage of inflammatory inhibition of all groups of test extracts has effectiveness comparable to the comparison group. EADP group 200 mg/kg BW is the best dose of extract as anti-inflammatory, where flavonoid compounds are thought to be responsible for decreasing the volume of inflammation in the legs of test animals.

Keywords: Papaya leaves (Carica papaya L.), plethysmometer, anti-inflammatory, 1% percentage of carrageenan, diclofenac sodium.

I INTRODUCTION

Indonesia is one of the countries that have diverse biodiversity. The diversity of plants owned by Indonesia ranks the second highest after Brazil. Seventy-five percent of the plants in the world can be found in Indonesia. This means that of the 40,000 species of flora that exist in the world, as many as 30,000 species can be found in Indonesia. Nine hundred and forty of them are plants that have medicinal or herbal properties [1]. From time to time traditional medicine has experienced an increasingly increasing development, especially with the emergence of the issue of returning to nature (back to nature) as well as the prolonged economic crisis which has reduced people's purchasing power. While many people assume that the use of traditional medicines is relatively safer than synthetic drugs. However, it does not mean that traditional medicines do not have adverse side effects. It is necessary to know adequate information about the accuracy of the dosage/dose, time of use, method of use, correct selection of materials, and selection of traditional medicines for certain indications so that their use is optimal. So it is not true, if said traditional medicine does not have side effects, however small the side effects remain, it can be minimized if sufficient information is obtained [2]. One type of plant used as traditional medicine is papaya leaves from the family Caricaceae. Papaya leaves are one of the plants that are often used for treatment for the community. Papaya leaves have long been used by community groups for treatment, such as malaria medicine, appetite enhancer, worm medicine, kidney stone medicine, shed menstruation, and pain relief [3]. Papaya leaves contain various compounds such as flavonoids,
enzymes papain, saccharose, dextrose, cellulose, protein, carbohydrates, calcium, phosphorus, iron vitamin A, vitamin B1, vitamin C, water and calories. Flavonoids are compounds that can protect lipid membranes from damage and inhibit the cyclooxygenase I enzyme, which is the first pathway for the synthesis of pain mediators such as prostaglandin. Papaya leaves contain various kinds of enzymes, one of which is the enzyme papain has an activity as an analgesic and anti-inflammatory [4].

Inflammation is a normal protective response to tissue injuries caused by physical trauma, destructive chemicals, or microbiological substances. In the acute form is characterized by classic signs, namely: pain (dolor), heat, redness (rubor), swelling (tumor), and loss of function (functionolesa) [5]. At present, there are various drugs used to treat inflammation. The anti-inflammatory non-steroidal groups can cause stomach or intestinal ulcers that sometimes may be accompanied by anemia due to blood loss, and kidney disorders [6]. Based on the description above, the researchers are interested in examining the anti-inflammatory activity of papaya leaf water extract obtained by inundation, and also to find the proper dosage as an anti-inflammatory which is observed through a decrease in edema volume in the soles of rat carrageenan-induced by 1%.

II METHODOLOGY

The method used in this study is an experimental method which includes preparing and collecting samples, processing samples, making simplicia, making extracts inundated using water solvents, testing the content of chemical compounds contained in simplicia and extracting water from papaya leaves (Carica papaya L.), preparation of test animals and testing of anti-inflammatory effects using a plethysmometer by giving suspense extract of papaya leaf water orally to male Wistar rats which had been induced by 1% carrageenan as artificial inflammatory inducers. The results of the research data were analyzed using Statistical Product and Service Solution (SPSS) version 20.0.

The material used in this research is fresh papaya leaves. The leaves are separated from fouling and then washed thoroughly then drained and weighed, obtained a wet weight of 5 kg, then the papaya leaves are dried in a drying cabinet at ±40°C until dry. Simplicia that has been dried is blended to powder, weighed and a simplicia weight of 600 gr is obtained. Then put into a tightly closed container and stored at room temperature. Some dry simplicia used to phytochemical screening, and some dry simplicia was extracted by infundation method for 15 min at 90°C, and then evaporated until a thick extract was obtained with a constant weight.

III RESULT AND DISCUSSION

Plant Identification
The results of plant identification carried out at the research center "Herbarium Medanese (MEDA)" University of North Sumatra, showed that the plants studied were papaya leaves (Carica papaya L.). Papaya leaf was taken from Garu Dua Street in Medan. Papaya leaf collection is done purposely, that is without comparing with other regions.

Extraction
From the results of extraction of simplicia, the percent yield was obtained which was 15.6%.

Characteristic Examination
The results of organoleptic examination of fresh leaves of papaya are papaya leaves are single leaves, large, branched, also have tapered leaf tips, long and hollow leaf stalks. The results of checking the characteristics of papaya leaf simplicia can be seen in the Table 1.

Table 1 The results of examination of the simplicia characteristics of papaya leaves

<table>
<thead>
<tr>
<th>Examination</th>
<th>Levels obtained (%)</th>
<th>Requirements MMI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>water content</td>
<td>8.9</td>
<td>&lt;10</td>
</tr>
<tr>
<td>the juice content dissolves in water</td>
<td>51.4</td>
<td>≥34.5</td>
</tr>
<tr>
<td>soluble juice levels in ethanol</td>
<td>10.2</td>
<td>≥9</td>
</tr>
</tbody>
</table>

From the results of the inspection that has been carried out, the determination of the moisture content is 8.9%, which is fulfilling the requirements, where the MMI requirement is <10%. In determining the level of juice where the content of soluble juice in the water obtained a weight of 51.4% and the content of soluble in ethanol with a weight of 10.2%, which has met the requirements of MMI, where the MMI requirement for water-soluble juice content ≥34.5% and Ethanol soluble levels of Ethanol ≥9%. The examination of the water content is intended to determine the water content in a simplicia, the determination of the level of water-soluble juice to determine the amount of compounds that can be dissolved in water. Determination of soluble levels of ethanol was carried out to determine the content...
of chemical compounds dissolved in ethanol [7].

Phytochemical Screening
The results of phytochemical screening of simplicia powder and papaya leaf water extract showed results that can be seen in Table 2.

Table 2 The results of simplicia powder phytochemical screening and papaya leaf water extract.

<table>
<thead>
<tr>
<th>Examination</th>
<th>Simplicia Powder</th>
<th>Extract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aconitin</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tanin</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Triterpen/Steroid</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Flavonoid</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Alkaloid</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Glikosida</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Based on the results of phytochemical screening from simplicia powder and papaya leaf water extract (Carica papaya L.), it contains alkaloid compounds, steroids/triterpenoids, glycosides, tannins and flavonoids. The compounds that have anti-inflammatory activity are flavonoids. From various research results reported, the chemical content it has its anti-inflammatory properties are flavonoids. Flavonoids can inhibit cyclooxygenase or lipoxygenase and inhibits the accumulation of leukocytes in the area so that it can be anti-inflammatory [8]. Based on result from Ramadhani and Sumiwi, it is found that the compound groups are inhibits in inflammation in testing anti-inflammatory activity of the five plants these are Flavonoid.

Anti-inflammatory Test
Testing the anti-inflammatory effect is carried out using a plethysmometer, with the principle of measurement based on the law "Archimedes". This test uses a water extract of papaya leaves with varying doses of 50 mg/kg body weight, 100 mg/kg body weight, 200 mg/kg body weight and uses a comparison of non-steroidal anti-inflammatory drugs sodium diclofenac 6.3 mg/kg body weight. Inflammatory induction was carried out chemically using 1% carrageenan solution which was injected sub plantar in the rat's foot as much as 0.1 ml. The formation of inflammation by carrageenan produces acute inflammation, and does not cause tissue damage, although inflammation can last for 300 min and gradually decrease for one day. From changes in volume of mouse feet can be calculated percent inflammation in rat feet. Changes in mouse foot volume and percent inflammation are directly proportional. If the change in volume of large rat feet, then percent inflammation is also large (Figure 1).

Based on the graphic, the measurement of volume of edema on male Wistar rat feet at 30 min shows the induction group with the EADP test group all doses did not differ significantly \( p < 0.05 \) but the induction group with the comparison group showed differences significant \( p < 0.05 \), at 30 to 120 min, the comparison group with all the test groups showed a significant difference \( p < 0.05 \), thus the comparison group had begun to give effect to time of 30 min, while the test group dose was 200 mg/kg BW and 100 mg/kg BW with the new comparison group showed a non-significant difference in time of 150 min \( p > 0.05 \), this indicates that EADP dosage dosages of 200 mg/kg BW and 100 mg/kg BW have begun to show effects the same as comparison. In 180 to 270 min all the test groups showed significant differences \( p < 0.05 \) with the induction group, and the comparison group did not differ significantly from all EADP preparatory test groups \( p > 0.05 \), however, in the 300 min the two test groups EADP preparations showed a significant difference with the comparison group and induction group \( p < 0.05 \).
Diclofenac sodium works by cyclo-oxygenase inhibitors, diclofenac sodium is used for long-term treatment of arthritis, rheumatoid arthritis, osteoarthritis and ankylotic spondylitis, more potent than indomethacin or naproxene [9]. Chemical compounds contained in papaya include potassium, magnesium, and antioxidants such as carotene, vitamin C and flavonoids, enzyme, alkaline papaya, and carpein and papain enzymes. Compounds that function as anti-inflammatory are flavonoids. This is because flavonoids can inhibit the enzyme cyclo-oxygenase, lipoxygenase and leukocyte accumulation [3]. This is in accordance with the results of simplicia phytochemical screening and papaya leaf water extract in this study which also shows the presence of flavonoids which are thought to have anti-inflammatory activity. The mechanism of flavonoids inside inhibit inflammation through two way, the first inhibits release arachidonic acid and secretion of the lysosome enzyme from neutrophil cells and endothelial cells, and the second inhibits the exudation phase and the phase proliferation of inflammatory processes. Inhibited release of arachidonic acid from inflammatory cells will cause lack of availability arachidonic substrate for the cyclooxygenase pathway and the lipoxygenase pathway, which is on will eventually suppress the amount of prostaglandins, prostacyclin, endoperoxide, thromboxane on one side and hydroperoxide acid, acid hydroxyecosatetraenoate, leukotriene on the side other [10].

CONCLUSION

Based on data from the results of research that has been done, it can be concluded that water extract of papaya leaves (Carica papaya L.) contains secondary metabolites, namely alkaloids, tannins, flavonoids, glycosides, steroids / triterpenoids. Papaya leaf water extract (EADP) has an anti-inflammatory effect on the decrease in uedema volume in the feet of male Wistar mice carrageenan-induced 1%. The most effective dose of papaya leaf extract (EADP) as anti-inflammatory in a row is a dose of 200 mg/kg BW, 100 mg/kg BW, and 50 mg/kg BW.

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REFERENCE