IAMSPH 3 (1) (2022) Pages:. 133-139

Journal homepage: https://pcijournal.org/index.php/iamsph

International Archives of Medical Sciences and Public Health

Published: Pena Cendekia Insani

Effectiveness Of Antipyretic Leaf Extracts Of Frown (Ipomoea Pescaprae L.) In Rats

Fahma Shufyani[1], Ani Rahmadhani Kaban[2], Saiyidatul Fadhilah Pane[3]

[1,3]Department of Pharmacy, Institut Kesehatan Helvetia Medan
[2] Department of Nursing, Institut Kesehatan Helvetia Medan

Article Info

Article history:

Received : 28 October 2021
Revised : 27 December 2021
Accepted : 30 January 2022

Keywords:

Katang-katang leaves (Ipomoea pescaprae L.), Fever, Bread Yeast, Rat

ABSTRACT

Fever is a condition where the body temperature is above normal (Wardiyah et al., 2016). Normal human body temperature ranges from 36-37°C, fever can exceed 37°C (Kurniati, 2016). The purpose of this study was to determine the fever-reducing effect of Katang-Katang leaf extract (Ipomoea pescaprae L.) on rats induced with baker's yeast. The method used in this research is experimental laboratory. The test animals used were 25 rats which were divided into 5 treatment groups, each group consisted of 5 rats. The positive control group used paracetamol 500 mg/kgBW, the negative control group used 1% CMC Na and the EEDK treatment group with doses of 100, 200, 300 mg/kgBW given orally. Mice were induced with 0.2 ml baker's yeast subcutaneously (s.c). Measurements of the rectal temperature of rats were carried out before and after yeast administration after treatment in consecutive tests at 4, 8, 12, 16 and 20 minutes. with EEDK at doses of 200 and 100 mg/kgBW, while paracetamol gave a greater decrease in rectal body temperature in rats than at a dose of 300 mg/kgBW. The results of the analysis showed that EDK doses of 100, 200, and 300 mg/kgBW did not have a significant difference with paracetamol at a dose of 65 mg/kgBW (P>0.05). It can be concluded that EEDK has the same effect as reducing fever in rats but not better than paracetamol. Suggestions for further researchers to carry out this research into dosage form and measure its toxicity.

Corresponding Author:

Fahma Shufyani,
Department of Pharmacy
Institut Kesehatan Helvetia Medan
Email: fahmaapotekerunand@yahoo.com

1. INTRODUCTION

Fever is one of the most common signs of illness. Fever is the reason behind 15-20% of patient visits in primary health care facilities or emergency units (Barbi et a., 2017). Febrile seizures are seizures that occur at an increase in body temperature of 38 ° C or more caused by processes outside the brain. Most febrile seizures occur in children aged 6 months to 5 years.

The hallmark of a febrile seizure is that the fever precedes the seizure. At the time of the seizure the child was still feverish and after the seizure the child immediately regained consciousness (IDAI, 2014).

Handling fever is divided into two, namely treatment without drugs (non-pharmacological therapy) and with drugs (pharmacological therapy). Handling without drugs is carried out by giving special treatments that can help lower body temperature, including giving fluids, using compresses, and avoiding wearing too thick clothes (Kristiyaningsih et al., 2019). Handling with drugs is done by giving antipyretic drugs that can reduce body temperature by various mechanisms (Lubis et al., 2016).

Antipyretics are included in the class of drugs that have the target of lowering body temperature (Journalis et al., 2015). Antipyretics work by inhibiting the cyclooxygenase (COX) enzyme and reducing the amount of PGE2 in the hypothalamus. Antipyretics are very easy to get freely in pharmacies, supermarkets, and grocery stores. Unfortunately, when people buy drugs outside pharmacies, people do not get complete information about these drugs. The absence of important information for example about the rules for using drugs, dosages, and side effects can have a bad effect on the patient. Paracetamol can cause allergic skin reactions and can cause liver problems if used long term (Bebenista et al., 2014).

Katang-katang (Ipomoea pescapre L.) is a creeping wild plant usually found in Indonesia and grows in coastal areas. Katang-katang is traditionally used by the community as an alternative medicine, one of which is used to treat bleeding in pregnancy by drinking boiled water. Many researchers have conducted research on the use of katang-katang leaves, one of which is as an antioxidant (Dahlia, 2018) which contains flavonoids and gives the result that the ethanol extract of katang-katang leaves has activity capable of inhibiting free radicals with a value of up to 46,774 (Dahlia, 2018) .

Research on the effectiveness of katang-katang leaves has been tested, one of which is used as an antibacterial because it contains flavonoids in it (Etin, 2021), and there is also research that leaves katang-katang to inhibit pain because it contains flavonoids in it (Dahlia, 2018). Secondary metabolites contained in katang-katang leaf plants are flavonoids, alkaloids, saponins, and tannins (Dahlia, 2018).

This study used rats induced using baker's yeast and paracetamol as a comparison, while CMC Na 1% as a negative control and katang-katang leaf extract as a treatment group with doses of 100 mg/kgBW, 200 mg/kgBW, 300 mg/kgBW (Junita .H, 2020).

2. RESEARCH METHODE

This type of research is an experimental laboratory or can be referred to as true experimental laboratories. The purpose of this study was to determine the antipyretic activity of EEDK extract in rats induced by baker's yeast.

According to (Notoatmojo, 2014) The population is the total number of samples to be studied. This study used a population of katang-katang leaves (Ipomoea pescaprae L.). The sample is an object under study which is considered to represent the entire population (Notoatmojo, 2014). This study used a leaf sample of katang-katang (Ipomoea pescaprae L.). According to (Fredrer, 1967), the sample determination formula for experimental tests is as follows:

$$(t-1)(n-1) \geq 15$$

Information:
t : Number of treatments
n : Number of samples for each treatment
With this formula, the number of samples for each group is a minimum of 5 rats. A total of 25 rats. The animals to be used were healthy rats weighing 20-30 g divided into 5 groups, where each group contained 5 rats consisting of 1 negative control group (CMC-Na 1%), 1 comparison group (Paracetamol) and 3 test groups. (dose variants of Suspension EEDK 100, 200, 300 mg/kgBW).
Before being treated, all rats were acclimatized for approximately one week to adjust the environment, control health and body weight and uniform food (Sabina, 2009 in Yolanda, 2017).

The sample used katang-katang leaves. Katang-katang leaf samples were taken at the Historical Beach of Perupuk Kec. Fifty, Kab. Coal, North Sumatra Province. Sampling was carried out purposively, namely a sampling technique without comparing with the same sample from other areas. This sampling method uses the criteria that have been selected by the researcher in selecting the sample.

The data obtained from the increase in temperature and % pyrex inhibition were then analyzed for normality and homogeneity tests using a statistical computer program, Statistical Product and Service Solutions (SPSS). If the % pyrexia inhibition data has met the requirements for normality and homogeneity, namely p value > 0.05, a one-way analysis of variance (ANOVA) parametric test can be performed with a 95% confidence level. This test was carried out to compare the group averages, if there was a significant difference with a p value <0.05 then the LSD post hoc test was continued. Meanwhile, independent t test was used to analyze the temperature rise. The test can show whether there is a significant difference between the non-induced group and the yeast-induced group of 10 ml/kgBW. The results will be considered statistically significant if the p value < 0.05

3. RESULT AND ANALYSIS

Plant Identification Results

The identification results indicate that the sample belongs to the family. The results of taking Katang-katang leaves were taken at the Historical Beach of Perupuk Kec. Fifty, Kab. Coal, North Sumatra Province weighing as much as 5 kg which has been separated from the trunk. The fresh leaves were dried to obtain a dry simplicia weight of 1.5 kg and the dried leaves were blended to become simplicia powder weighing 1.2 kg.

Sample Processing

Katang-katang leaves that have been taken, sorted wet, weighed 5000 grams then cleaned of impurities, washed with running water, drained. Furthermore, katang-katang leaves were dried under an incandescent lamp, then sorted dry, weighed 1500 g, then the simplicia was blended into powder with a weight of 1200 g and put in a tightly closed container.

Making Katang-katang Extra Leaves

In the manufacture of katang-katang leaf extract as much as 500 g of randu leaf powder was macerated using 3,75 liters of 96% ethanol solvent for 5 days, then the maserate was separated, the pulp was macerated again with 1,25 liters of 96% ethanol solvent for 2 days, the macerate is separated. All maserates were combined and evaporated using a rotary evaporator to obtain 96% ethanol extract of katang-katang leaves. Then followed by evaporation using a water bath, to prevent damage to the active compounds and to avoid microbial contamination, the katang-katang leaf extract was stored in a refrigerator at a temperature of 2-8°C. The final result of the thick extract of katang-katang leaves obtained was 90.61 gr.

Macroscopic Examination

Based on the results of organoleptic examination, the characteristics of katang-katang leaves are as shown in the table below:

Table 4.1. Macroscopic Observation Results

Checked Components	Fresh Leaves	Simplicity
Form	Tapered Shape, Push And Round	Powder
Color	Green	Dark Chocolate
Smell	Typical	Typical
Flavor	Bitter, Slightly Crude	Bitter, Slightly Crude
Size	2-3 cm	Fine

Characterization of Katang-Katang Leaf Simplicia

The results of the examination of the characterization of katang-katang leaf simplicia powder which included examination of water soluble extract content, ethanol soluble extract content, total ash content and acid insoluble ash content.

Determination of the water content of simplicia was carried out with a moisture analyzer on the simplicia leaves of katang-katang. Based on the results of the characterization of the water content, 5.04% can be obtained. Moisture content based on MMI (Materia Medica Indonesia) is not more than 10%. The purpose of determining the water content is to determine the amount of water contained in the simplicia and to maintain the quality of the simplicia which may have fungi or microbes in it.

The results obtained water soluble extract content of 18.2949% and ethanol soluble extract content obtained by 14.4685%. The determination of the water soluble extract content was higher than the ethanol soluble extract content, meaning that the compounds dissolved in water were higher than the compounds dissolved in ethanol.

The results obtained total ash content of 2.51% and acid insoluble ash content obtained 0.93%. Determination of total ash provides an overview of mineral content from the initial process to the formation of extracts, while determination of acid insoluble ash is to determine the content of compounds that are insoluble in acid (Mayasari et al, 2018).

Phytochemical Screening

Phytochemical screening of simplicia powder and ethanol extract of katang-katang leaves was carried out to determine the chemical compounds contained in the simplicia. In this study, phytochemical screening was carried out on the simplicia powder of katang-katang leaves. The purpose of phytochemical screening is to detect secondary metabolites present in simplicia. This test is carried out by taking a small sample and adding reagents/reagents according to the type of secondary metabolites to be identified. Based on the results of phytochemical screening, the simplicia powder of katang-katang leaves was positive for alkaloids, flavonoids, saponins, tannins, steroids/triterpenoids. By obtaining the results of phytochemical screening, it is possible to determine the function of each secondary metabolite and can support the pharmacological effects that may occur in plants.

Observation Result

This study used 5 treatment groups, namely the negative control group using 1% CMC Na, the positive control using paracetamol 65 mg/kgBW, the EEDK test group with treatment doses of 100 mg/kgBW, 200 mg/kgBW, and 300 mg/kgBW.

Antipyretic Effect Test

In this study, all test animals were induced first with baker's yeast so that the animals to be tested experienced an increase in body temperature or called fever. Acquired fever caused by the presence of gram-positive bacteria can cause fever by triggering an inflammatory reaction by releasing pyrogens endogenous, part of the bacteria is mucopeptide (Feuer and de la Iglesia, 2019). Yeast cell walls of Saccharomyces cerevisiae contain manna polymers which can stimulate the secretion of pyrogenic cytokines such as TNF- which then initiates the pyrogenic stage in the blood circulation. Peripheral pyrogenic substances can provide a fever response in the hypothalamus by increasing the synthesis of COX products from arachidonic acid (especially PGE2) in the thermoregulatory center of the brain to increase thermoregulation from the set point (Ataoglu et al., 2000).

In this study, 5 treatment groups were used, namely the negative control group using 1% CMC Na, the positive control using paracetamol 65 mg/kgBW, the EEDK test group with treatment doses of 100 mg/kgBW, 200 mg/kgBW, and 300 mg/kgBW.

In (Figure 4.1) shows an increase in temperature in rats after being induced using Bread Yeast after 4 hours, rats that already have a fever are then given EEDK and paracetamol with each dose. To see the power of EEDK and Paracetamol in lowering body temperature. The results of the measurement of the rectal temperature of the rats in (Table 4.2) showed variations in the fever temperature of each group after treatment. The decrease in temperature that varies is thought to be due to endogenous factors of each rat that are individual to fever-causing agents such as stress and in rats due to treatment in measuring the rectal temperature of rats repeatedly is a disturbing factor that causes an increase in the temperature of rats.

The high and low temperature indicates °C of fever experienced by each rat. The higher the increase in the rectal temperature of the rats, the higher the °C of fever that the rats will experience, and vice versa. After each treatment was given, the average value was observed, if there was a decrease in the rat's rectal temperature, it meant that the fever had started to fall, in other words, the antipyretic effect increased. This can be seen in (Table 4.2) and (Figure 4.2) the results of the decrease in the average rectal temperature of rats in the 65 mg/kgBW paracetamol treatment group experienced the best decrease in temperature in the 20th minute, which was 36.1°C. A nice drop in temperature occurs because paracetamol has an antipyretic effect. The

mechanism of action of the drug paracetamol is able to inhibit cyclooxygenase in the brain so that paracetamol is effective in reducing fever. In the EEDK group of 300 mg/kgBW in the 20th minute, it was 37.0°C. This group experienced a decrease in temperature that was close to the decrease in paracetamol temperature, this was because the EDK 300 mg/kgBW was in a higher dose concentration and had more opportunities to bind to the receptor so that the effect was better than the EDK 200 mg/kgBW and EEDK 100 mg/kgBW. However, the two groups of 200 mg/kg BW EDK at the 20th minute, which is 37.1°C and the EDK 100 mg/kgBW at the 20th minute, which is 37.3°C, have an antipyretic effect but are not effective because the temperature drop is smaller. . Meanwhile, the smallest 1% CMC Na gave effect in lowering body temperature compared to the other treatment groups, which was 38.0°C at 20 minutes. This is because 1% Na CMC does not have an antipyretic effect.

In (Figure 4.3) provides a decrease in the average temperature of rats between the treatment groups of the five treatment groups. In the first 4 minutes of temperature measurement, the treatment group did not show an increase in the average temperature of the rats. This is presumably due to the antipyretic effect in the treatment group that has not worked, or the effect of pyrogens from baker's yeast that is still working is more dominant. In the paracetamol treatment group, the average decrease in temperature began to appear in the 4th minute and the largest average decrease occurred at the 12th minute. The EEDK of 300 mg/kgBB the average temperature decrease began to appear at the 8th minute, but the average temperature decrease was greatest at the 20th minute. While EEDK 200 mg/kgBW and EEDK 100 mg/kgBW the average temperature decrease began to appear at the 16th and 20th minutes, but not for the 1% Na CMC treatment group, the average temperature did not decrease at the 15th minute. 8 and 1% CMC Na were the treatment groups with the smallest average temperature drop, which was at 20 minutes.

In this study, EEDK was shown to have an antipyretic effect in rats induced with baker's yeast. The antipyretic effect of EED is thought to be due to the presence of flavonoid compounds. Flavonoids work to trigger the formation of prostaglandins, prostaglandins, increasing body temperature. If prostaglandins are not inhibited, there will be an increase in body temperature which will cause fever.

Several studies have proven that plant extracts containing flavonoid compounds have potential antipyretic activity (Belangoy and Mariano, 2016; Zulfa et al., 2017; Abbasi et al., 2018). Plant extracts containing flavonoid derivatives such as pinocembrin, kaempferol and quercetin have antipyretic effects by inhibiting inflammatory mediators and pyrogenic cytokines (Abbasi et al., 2018). The antipyretic effect was confirmed by the finding that flavonoid derivatives were reported to be able to inhibit the activity of COX so that the synthesis of prostaglandins was also inhibited (You et al, 1999). Based on this description, the antipyretic effect may also be due to the anti-inflammatory effect which is the inhibition of prostaglandin synthesis.

4. CONCLUSION

1. Ethanol extract of katang-katang leaves can reduce body temperature in rats.
2. The ethanol extract of katang-katang leaves at a dose of 300 mg/kgBW has the same effect as paracetamol with an average temperature reduction at 4 minutes = 38.1°C, 8 minutes = 37.8°C, minutes 12th minute = 37.6 °C, 16th minute = 37.4 °C, 20th minute = 37.0 °C.

3. The ethanolic extract of katang-katang leaves can reduce body temperature in rats, but not better than paracetamol 65 mg/kgBW with an average temperature decrease at the 4th minute = 37.6 °C, the 8th minute = 37, 1 °C, 12th minute = 36.8 °C, 16th minute = 36.4 °C, 20th minute = 36.1 °C and showed no significant difference to the ratio of paracetamol 65 mg/kgBW ($p>0.05$).

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