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Antipyretic Effectiveness Test of Ethanol Extract of Kaempferia Galanga L. Rhizoma in DPT Vaccine-Induced Wistar Rats

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ABSTRACT

Introduction: Antipyretics is another name for no fever, which is where the body temperature increases, which can be caused by infection, immunization factors.
Objective: This study was to determine the effect of extracting kaempferia galanga rhizomes on temperature reduction in wistar rats of fever induction DPT vaccine.
Methods: The DPT vaccine has side effects, one of which is fever, particularly in the proximal portion. Thirty-six male Wistar rats were divided into six groups. Group 1 was the normal group, uninjected with DPT vaccine. Groups II, III, IV, V, and VI were induced with 0.2 ml of DPT vaccine intramuscularly. Group II, the negative control, was given 0.5% CMC-Na. Group III served as the positive control with 5 ml of paracetamol suspension. Groups IV, V, and VI were given 0.5%, 0.75%, and 1% galangal extract, respectively. The temperature of each rat was measured every 30 minutes for 180 minutes.
Results: The antipyretic effect began to be seen in the 60th minute. The average temperature reduction of various groups was 0.04◦C, 0.04◦C, 0.29◦C, 0.25◦C, 0.22◦C and 0.28◦C. Ethanol extract of kencur rhizome contains flavonoid, saponin and terpenoid compounds. Ethanol extract of kaempferia galanga rhizome has the potential as an antipyretic or anti-fever, at a dose of 1% is the optimum dose used as an antipyretic.
Conclusion: Ethanol extract of kaempferia galanga rhizome contains flavonoid, saponin and terpenoid compounds, and has the potential as an antipyretic or anti-fever with an optimum dose of 1%.

Keywords : Antipyretic, kaempferia galangal L, DPT Vaccine, extract of the kaempferia galanga rhizome

INTRODUCTION

Antipyretics or often called anti-fever are symptoms of an infectious disease such as dengue fever, typhus, malaria, liver inflammation, and other infectious diseases. Antipyretics are a class of drugs for fever. Fever is actually the body's defense mechanism against germs, infections. When an infection occurs, our brain will raise the body's temperature standard above normal values so that the body becomes feverish. Antipyretic drugs work by lowering the temperature standard to normal values. The normal value of the human body is 36.5–37.5 degrees Celsius (Hastuti & Susi, 2016). In this modern society, people do not really know about the benefits that we can get from herbal plants for health, because people are more familiar with chemical medicines, either because of recommendations from doctors who more often give prescriptions to buy chemical medicines at pharmacies or because they are easily obtained at the nearest shop or stall, so that people are less

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aware of the special advantages that herbal plants have compared to the chemical medicines that they usually consume.

Plants that have potential as medicine are kaempferia galanga rhizomes. Kaempferia galanga rhizomes are widely known in society both as food seasonings or for treatment including coughs, nausea, swelling, boils, antitoxins such as bongkrek tempeh poisoning and mushrooms. In addition, it is efficacious for increasing endurance, eliminating colds, and fatigue, and as an analgesic (Hayati et al., 2015). There has not been much research on kaempferia galanga rhizome for antipyretics. This is what prompted researchers to conduct research on the antipyretic effectiveness test of ethanol extract of kaempferia galanga rhizome on white male wistar rats given DPT vaccine. Ethanol extract was chosen because it is easy and fast to work with and can attract active flavonoid substances.

MATERIALS AND METHODS

Study Design

This study used an experimental study, namely 36 male Wistar rats were divided into 6 groups. Group 1 is a normal group without DPT vaccine induction. Groups II, III, 1V, V and VI were induced by DPT vaccine 0.2 ML intramuscularly. Group II control (negative) did not receive drug treatment only given CMC-Na 0.5%. Group III as a positive control was given treatment with paracetamol suspension 5 ML / rat. Groups IV, V and VI were given 0.5%, 0.75% and 1% kaempferia galanga extract, the temperature measurement of each rat was carried out every 30 minutes for 180 minutes using an infrared thermometer. The study was conducted at the Pharmacology Laboratory of ITEKES Cendekia Utama Kudus.

Materials

Tools used Rat cage, animal scales, stop watch, infrared thermometer, sonde, sped, rotary evaporator. Materials used include, male white rats Wistar strain with a body weight of 200 grams, Galangal rhizome extract used for treatment tests, CMC-Na used as a negative control, 96% Ethanol functions for soaking the extract, DPT vaccine used as an agent to increase body temperature in rat, Paracetamol used as a positive control.

Extraction and Sample

Sample Processing Making powdered herbal medicine The kaempferia galanga rhizome is washed clean in running water, it functions to remove dirt such as soil, gravel that sticks to the rhizome. Then the kaempferia galanga rhizome is thinly sliced with a thickness of approximately 3 mm, then dried in a 40◦C oven for 72 hours. The dried herbal medicine is then ground by blending. Making kaempferia galanga rhizome extract Weighing the dried kaempferia galanga rhizome powder, adding 96% ethanol solvent, then soaking for 3 days, stirring occasionally. Every 24 hours it is replaced by filtering with filter paper, the filtrate is macerated again but with a new solvent and has the same concentration, then the extract is concentrated with a rotary evaporator (Kementerian Kesehatan, 2000). CMC Na Suspension 0.5% CMC-Na as much as 0.5 grams is put into a mortar containing 10 ml of warm distilled water. Stir until it expands then smooth until homogeneous. After that, it is diluted with distilled water until the total solution volume is 100 mL.

Determination of paracetamol dose In adult doses, paracetamol is given at a dose of 500 mg. The conversion dose from humans to rat is 0.018 The dose of paracetamol given to white male rat is in the form of paracetamol tablets made into powder with the calculation of 500 mg x 0.018 = 9 mg, so 100ml / 5ml x 9 mg = 180 mg of paracetamol that is weighed Making paracetamol suspension Weighing 180 mg of finely ground paracetamol then dissolved in 100 ml of CMC-Na. The volume given to rat is 5ml / day / rat orally. Determination of the dose of kaempferia galanga rhizome extract The dose of kaempferia galanga rhizome extract given orally to rat is: 0.5%, 0.75% and 1%. Diluted with 0.5% CMC-Na then given to rat orally 5ml/rat.

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Antipyretic Effectiveness Test

Antipyretic effectiveness test male white rat were fasted for approximately 6 hours after being adapted for 7 days in the research cage. Then 36 male white rat were grouped into 6 groups, each group consisting of 6 male white rat selected randomly. Namely C1 C2, C3, P1, P2 and P3 then each rat was weighed. Each male white rat of the Wistar strain before being treated had its temperature measured with an infrared thermometer by means of per rectum. Then the male white rat were given 0.2 ml of DPT vaccine per rat intramuscularly according to their group. Body temperature was measured after 3 hours of DPT vaccine administration. And given treatment according to their group 3 hours after checking the administration of the DPT vaccine.

Phytochemical Screening

Test for flavonoid compound content,1 gram of extract, add 5 ml of distilled water, then heat. Filter and then measure 1 ml of filtrate, add a few drops of sodium hydroxide solution. If a yellow color forms when added, the filtrate contains flavonoids (Muharrami et al., 2017).

Saponin content test, 1 gram of extract, add 10 ml of distilled water, heat with a test tube, cool then shake vigorously for 15 seconds, foam forms for no less than 10 minutes, when 2 N HCl is added the foam does not disappear indicating the presence of saponin compounds (Muharrami et al., 2017).

Steroid test, 1 mg of extract is put into a test tube and anhydrous acetic acid and concentrated sulfuric acid are added. If a green color is formed, it is positive for steroids, but if an orange color is formed, it is positive for terpenoid.

Statistical Analysis

Data analysis test using statistics After the data is obtained, the data is entered and processed using SPSS software. The data obtained is tested for homogeneity with the Test of Homogeneity of Variance and the normality test with the Shapiro-Wilk test. If the data is normally distributed and the homogeneity P> 0.05, then a one-way ANOVA Test Sig <0.05 analysis is carried out which is then continued with the post hoc test

RESULTS

Table 1 shows the results of phytochemical screening of secondary metabolites from ethanol extract of kaempferia galanga rhizome.

Table 1 Phytochemical screening test

Compound	Testing methods	Test results	Conclusion
Flavonoid	Mg and HCl Powder	Orange, yellow	+
Steroid	anhydrous acetic acid and concentrated sulfuric acid	Green	+
Saponins	Aquadest and Hcl 2N	There is stable foam or foam for less than 10 minutes	+

(+) contains the tested compound

The results of the average rectal temperature measurements in test animals before and after DPT vaccine injection and rectal temperature after administration of the test material. The change in rectal temperature at each time interval in each treatment group was obtained through the calculation of Δt, which is the difference in average temperature at 30 minutes after and 30 minutes before. The change in rectal temperature that occurred from the 30 minute to the 180minute was totaled to

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determine the antipyretic effect of each treatment group for 180 minutes can be seen in table 2 and 3.

Table 2 Average temperature in Rats

Group	Before treatment	After being vaccinated (t0)	Times (Minute)					
			30	60	90	120	150	180
C.1	36.31	36.25	36.38	36.36	36.40	36.41	36.50	36.35
C.2	36.35	37.43	37.48	37.46	37.44	37.41	37.33	37.25
C.3	36.38	37.51	37.08	36.83	36.71	36.66	36.43	35.81
P.1	36.45	37.55	37.35	37.80	37.05	36.85	36.71	36.63
P.2	36.35	37.61	37.25	36.78	36.56	36.38	36.30	36.25
P.3	36.25	37.75	36.91	36.60	36.41	36.36	36.00	35.75

In units of ◦c
C1 = normal group
C2 = Negative group
C3= Positive Group
P1= treatment dose 1 (0.5%)
P2= treatment on side 2 (0.75%)
P3= treatment dose 3 (1%)

Table 3 The variation in temperature observed in each treatment group over time

Group	Times (Minute)					
	30	60	90	120	150	180
C.1	-018	-0.06	-0.33	-0.18	-0.01	-0.08
C.2	0.06	0.08	0.03	0.11	0.25	-0.15
C.3	1.15	0.65	0.78	0.78	1.08	1.70
P.1	0.2	0.33	0.45	0.68	0.78	1.06
P.2	0.36	0.83	1.05	1.31	1.28	1.36
P.3	0.83	1.2	1.33	1.38	1.73	1.85

In units of ◦c
C1 = normal group
C2 = Negative group
C3= Positive Group
P1= treatment dose 1 (0.5%)
P2= treatment on side 2 (0.75%)
P3= treatment dose 3 (1%)

DISCUSSION

DPT vaccine In the Indonesian pharmacopoeia, 4th edition. Diphtheria vaccine is made from weakened diphtheria germ toxin (toxoid). It is usually processed and packaged together with tetanus vaccine in the form of DT vaccine, or with tetanus and pertussis vaccine in the form of DPT vaccine. Possible immunization reactions are usually mild fever, swelling and pain at the injection site for 1-2 days. Sometimes there are more severe side effects, such as high fever or seizures, which are usually caused by the pertussis element. If only DT (diphtheria and tetanus) is given, it will not cause fever. DPT vaccine can cause fever because the pertussis part is taken from all the germ cells (whole cells). This germ cell part is what causes the side effect of fever.

Antipyretic test of ethanol extract of kaempferia galanga rhizome on decreasing body temperature of rat must be carried out on experimental rat in fever condition, therefore artificial fever

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is needed to increase the temperature of experimental animals, namely by using DPT vaccine induction method of 0.2 ml. The results of temperature measurement in the table show the variation of average temperature in each group after being given treatment. The high and low increase in temperature indicates the degree of fever experienced by each rat. The higher the increase in temperature means the higher the degree of fever experienced by the rat, and vice versa if after treatment there is a decrease in the body temperature of the rat, it means that the fever is starting to decrease.

From the data obtained the results of temperature measurements in white rat the initial temperature of all treatment groups was relatively the same. After the DPT vaccine was injected intramuscularly into the rat, it showed that all rat were in a feverish condition. Except for the normal group which did not experience an increase in temperature, because it was not injected with the DPT vaccine, it can be seen in table 2 and 3.

Fever can be caused by the presence of pyrogens in the body and brain disorders or due to toxic materials that affect temperature regulation. The DPT vaccine is made from germ toxoids that are often used to strengthen the body's resistance to diphtheria, portusis and tetanus. But the DPT vaccine has side effects, one of which is increased body temperature. The part that can increase body temperature is the portusis (BPOM RI, 2008).

All test animals that have experienced an increase in body temperature of 0.6 ◦C can be categorized as having a fever (2010). The results of this study showed that the temperature of the test animals, namely male white rats of the Wistar strain, experienced an increase in fever above 0.06 ◦C so that it can be said that the test animals reached peak fever.This varying temperature increase may be caused by endogenous factors, namely vaccination factors, in each male rat that is individual to the fever-triggering agent and is greatly influenced by several non-physical or environmental factors. The presence of stress in rat due to repeated body temperature measurement treatments is one of the interfering factors that causes an increase in rat temperature. Variations in temperature measurement results can be understood because there is a diversity of sensitivity of each test animal which is a result of biological differences, namely the bioavailability and biochange of a drug. The fate of the drug in this case the administration of kaempferia galanga rhizome extract and paracetamol as a positive control, can be influenced by pathological factors that can cause the drug to decrease or increase. The decrease in drug effects may be a consequence of poor absorption in the digestive tract, blood vessels or increased excretion through the kidneys (Harvay and Pamela 2006)

The decrease in body temperature of rat between treatment groups above shows a decrease in body temperature in all six groups. In the first 30-minute temperature measurement, some treatment groups still showed an increase in temperature. This may be because the antipyretic effect works more dominantly. The antipyretic effect has begun to be seen in the 60th minute. The average decrease In the normal group experienced a decrease in temperature of -0.16 ◦C, the negative group 0.11 ◦C, the positive group 1.35 ◦C, the 0.5% dose treatment group 0.55 ◦C, the 0.75% dose treatment group 1.03 ◦C and the 1% dose treatment group 1.40 ◦C. the group that experienced the greatest average decrease in body temperature was the 1% dose treatment group.

Flavonoid compounds are thought to have a structure similar to paracetamol, namely both are phenol groups and have benzene rings (Syarifah L, 2010). In addition to flavonoid compounds, this study also found secondary metabolite compounds of steroids and saponins which are used for anti-inflammatory and antibacterial (Samanhudi et al., 2015) and are thought to be able to affect the decrease in body temperature in rat.

In addition to flavonoid compounds, this study also found secondary metabolite compounds of steroids and saponins which are used for anti-inflammatory and antibacterial purposes (Samanhudi et al., 2015) and are thought to be able to influence the reduction of body temperature in rat.

The largest group of flavonoids is characterized by having a pyran ring that connects the three-carbon chain with one of the benzene rings and the paracetamol effect is caused by the aminobenzene group (Fauziah, 2010). The antipyretic effect is because the ethanol extract of kaempferia galanga

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rhizome contains flavonoid compounds (Giri, 2017). Flavonoids have various bioactivities, the derived bioactivities include antipyretic, anti-inflammatory and analgesic effects. Flavonoids work as cyclooxygenase inhibitors. COX 2 functions to trigger the formation of prostaglandins which play a role in the inflammatory process and increase body temperature. If prostaglandins are not inhibited, there will be an increase in body temperature which will result in fever (Suwartayasa, 2013)

The ethanol extract of kaempferia galanga rhizome and paracetamol in the antipyretic test on rats used a 0.5% CMC-Na suspension, to suspend the ethanol extract of kaempferia galanga rhizome and facilitate the administration of the extract in test animals so that the concentration is in accordance with the dose given, the positive control was also dissolved using a 0.5% CMC-Na suspension and the negative control used a CMC-Na suspension.

In this study, paracetamol was used as a comparison because paracetamol is a drug that is often used for antipyretics. The paracetamol treatment group in this study showed a significant antipyretic effect in the paracetamol group, the decrease in body temperature of the rat had begun to appear at 30 minutes, but at 60 minutes there was only a significant decrease in temperature because the peak plasma concentration occurred in 30-60 minutes.

Paracetamol has a half-life of 180 minutes, in this study the research time used was only up to 180 minutes, so paracetamol had not worked perfectly, so that in the positive group the drug absorbed by the rat was slightly smaller when compared to the 1% dose group. It is suspected that the group responsible for antipyretic activity is flavonoids, which are able to inhibit the cyclooxygenase-2 enzyme which plays a role in prostaglandin biosynthesis so that the fever process can be inhibited.

The data presented were first tested for normality. The data were declared normal and homogen distributed because the sig value was >0.05. The ANOVA results indicate significant differences in the source of variation among the treatment groups. After the ANOVA, a post hoc test was performed to determine which groups had significantly different temperature reductions. The post hoc test results showed various comparisons between the treatments. In providing rational therapy, drug dosage is the most important factor, because either an under- or over-dosage will produce undesirable effects, and are often even dangerous (Lestari, 2001).

CONCLUSIONS

Ethanol extract of kaempferia galanga rhizome has the potential as an antipyretic or anti-fever. And the optimum dose of ethanol extract of kaempferia galanga rhizome that provides antipyretic activity is in treatment 3 with a dose of 1%.

Authors' Contributions

SF, KNM and AM contributed to the study design. SF and KNM contributed to the laboratory work carried out. Further, SF, KNM and AM contributed to the data analyses and article writing. All authors read and agree to the final version of the article.

Conflict of Interest

The authors have no conflicts of interest regarding this investigation.

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