SJP 5(1) (2024)

Sasambo Journal of Pharmacy

https://jffk.unram.ac.id/index.php/sjp

Antipyretic activity test of cucumber *(Cucumis sativus* L.*)* ethanol and methanol extract on male white mice *(Mus musculus)*

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DOI: https://doi.org/10.29303/sjp.v5i1.310

Article Info
Received : 24-08-2023
Revised : 19-05-2024
Accepted : 20-05-2024

Abstract: Cucumber plants are annual plants that grow in the lowlands or highlands. Cucumbers are easy to get and have lots of benefits, but the peel of the cucumber is still less desirable, so it becomes waste. On the peel of cucumber *(Cucumis sativus Linn)* showed the active compounds of saponins, phenolics, steroids, protein, calcium and flavonoids. Compounds that have an antipyretic effect are flavonoid compounds. The aim of the research was to determine the ability of the methanol and ethanol extracts of cucumber peels as antipyretics. This study was included in an experimental study by looking at the effect of methanol and ethanol extract of cucumber peels on male mice. The method used is chemical induction method. Forty male mice with body weight between 20-30 grams, divided into 8 groups: negative control, positive control, cucumber peel methanol and ethanol extract dose of 100 mg/kg BW, 200 mg/kg BW, 400 mg/kg BW. The decrease in temperature was observed for 180 minutes with an interval of 30 minutes. It is known that at 30 minutes it has shown a decrease in temperature, until at 240 minutes the temperature drop has reached normal temperature. The data obtained were analysed statistically with One-way ANOVA. The results showed that cucumber peel extract *(Cucumis sativus Linn)* could provide antipyretic activity at doses of 100 mg/kg BW, 200 mg/kg BW, and 400 mg/kg BW in peptone-induced male mice *(Mus musculus),* by injecting subcutaneously in the nape of the mice. The effective dose Cucumber peel of Ethanol and Methanol extract *(Cucumis sativus L.)* used to reduce the rectal temperature of male white mice is at a dose of 400 mg/Kg BW

Keywords: *antipyretic, cucumber peel methanol and ethanol extract, Mus musculus.*

Citation: Arifianto N., Saputri C.A., Retnosari F., Meidina H., and Wahyuni W. (2024). Antipyretic activity test of cucumber *(Cucumis sativus* L.*)* ethanol and methanol extract on male white mice *(Mus musculus). Sasambo Journal of Pharmacy, 5*(1), 20-25. doi: https://doi.org/10.29303/sjp.v5i1.310.

Introduction

In accordance with their natural nature, humans always try to fulfil their needs by utilizing everything around them, including for food and medicine needs. Indonesia has various kinds of natural wealth, including a wealth of plants which include medicinal plants. The use of medicinal plants has been carried out by the community for a long time and has been passed down from generation to generation to the next generation which we know as traditional medicine (Susanty, 2003).

The use of plants as traditional medicine is still commonly used by people in Indonesia, especially in rural areas which are still rich in plant diversity (Saumantera, 2004). There are several benefits that can be derived from the use of traditional medicine, namely: the price is relatively cheap, easy to obtain

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because there are usually many medicinal plants in rural areas, even medicinal plants can be grown alone in the yard of the house, safe to use because the side effects caused by traditional medicines are relatively small (Susanty, 2003).

Cucumber plants can be used as seasonings or commonly known as spices, cooked into vegetables, cosmetic ingredients, and used as medicine known as traditional medicine. One plant that has many benefits is cucumber. Cucumber is one of the many fruit vegetables consumed fresh by Indonesian people. In society, it is often found that cucumbers are used as food in the form of various preparations or can be eaten directly without cooking. In addition, cucumbers can also be used as traditional medicine because the content contained in cucumbers is very useful in treating diseases. An example of research that was conducted by Resita Putri (2020) in a study entitled "Test of Anti-cholesterol Potency of cucumber peel methanol and ethanol extract "which stated that saponin compounds, flavonoids in cucumber peel can be used as anti-cholesterol. To find out more about the benefits of cucumber peel, there needs to be ongoing research on the benefits of cucumber peel.

The plant used is cucumber peel *(Cucumis sativus L.)* because there is often a lot of waste from cucumber peel which is not utilized properly by the community due to lack of knowledge about the benefits of cucumber peel. Cucumber peel *(Cucumis sativus L.)* contains flavonoids which can be used as an antipyretic (Depkes RI, 2001). And there is no research on cucumber peel antipyretics *(Cucumis sativus L.)* so this research is needed to find out the antipyretic benefits of cucumber peel *(Cucumis sativus L.)*. In line with the development of science and the development of today's modern medical efforts, traditional medicines are also expected to play a role in efforts to improve health standards.

Based on the description above, the researcher is interested in conducting further research regarding the antipyretic test of methanol and ethanol extract of cucumber peel *(Cucumis sativus Linn)* in male mice *(Mus muscullus)* induced with graded doses of cucumber peel methanol and ethanol extract, namely 100 mg/kg BW, 200 mg/kg BW and 400 mg/kg BW.

Materials and Methods

Materials

The tools used are mouse cage, beaker glass, measuring flask, 1 ml syringe (Terumo 1 ml), stir bar, digital thermometer *(ThermoOnemed)*, stopwatch, sterile cotton, or tissue, stirring rod, vessel, rotary evaporator, porcelain crusher, weighing bottle, desiccator, water bath or water bath, porcelain crusher *(moisture tester)*, weighing bottle *(dry shrinkage tester)*, analytical balance *(Ohaus PA224)*, male mice with body weight between 20-30 grams and age 3-4 months, and evaporator cup. The ingredients are 500 mg acetaminophen, cucumber peel simplicia, methanol, 70% alcohol, distilled water *(water for injection)*, and 5% peptone.

Methods

Preparation of Ingredients for Cucumber Peel Simplicia

The material used is green cucumber peel, which is still fresh and ripe. The cucumber peel obtained is then cleaned of dirt and washed with running water. After the cucumber peel is clean, it is drained to reduce or remove the water content. Then the cucumber peel is chopped to facilitate the process of drying and smoothing.

The next process is that the cucumber peel is dried in aerated manner and protected from direct sunlight to avoid damaging the bioactive content of the cucumber peel (Nyoman et al., 2015). After the cucumber peel is dry, sort it dry and then grind it in a blender.

Extraction method

Weigh 200 grams of cucumber peel powder sample, then put it into the maceration vessel. Slowly pour 70% ethanol dan methanol solvent with a ratio of 1:10 (Nyoman et al., 2015), namely 2000 ml into a maceration vessel containing cucumber peel simplicia powder.

Allow the liquid to soak the simplicia powder for 3 x 24 hours at room temperature (15°-30°C) protected from sunlight, while stirring occasionally, strain using a filter and then collect the filtrate. The filtrate was evaporated using a rotary evaporator with a temperature of 70°C at a speed of 50rpm then concentrated with a water bath to obtain a thicker extract.

Drying shrinkage determination test

The extract was weighed carefully as much as 1 gram to 2 grams and put into a closed shallow weighing bottle which had previously been heated at 105°C for 30 minutes and had been tare. Before weighing, the extract is evenly distributed in the weighing bottle, by shaking the bottle until a layer is less than 5 mm to 10 mm thick, then placed in the oven. Open the lid, dry at 105ºC until constant weight. Before each drying, allow the closed vial to cool in a desiccator to room temperature. Then dry again at the specified temperature until the weight remains (Depkes RI, 2000).

Making Peptone Inducing Solution 5%

Weigh 5 grams of peptone, put it in a 100 ml volumetric flask and add aqua pro injection little by little until dissolved. Then the volume is sufficient with aqua pro injection up to 100 ml.

Preparation of 500 mg Acetaminophen Suspension

Crush Acetaminophen 500 mg tablets, dissolved in 50 ml aqua pro ad injection.

Preparation of Cucumber Peel Ethanol and Methanol Extract Solution

Weigh the extract as much as 500 mg. Add aqua pro injection little by little while stirring. After being homogeneous, add 50 ml of aqua pro ad injection.

Antipyretic Test

Prior to treatment, the test animals were adapted to the experimental room for approximately 18 hours, then fasted for 6 hours before treatment, but were still given drinking water. The test animals were then divided into 5 groups, each consisting of 5 male white mice (Ratna, 2017). Weigh the test animal using a scale. Then calculate the dose of mice. We first measured the rectal temperature of male white mice to find out the initial temperature before being induced by peptone. Then the mice were induced using 5%peptone, by injecting 0,22 mL of 5% peptone subcutaneously according to the body weight of male white mice. To find out the increase in temperature due to being induced using peptone, half an hour after that, measure the rectal temperature of male white mice. After measuring the temperature, each group received treatment with subcutaneous extracts with different doses, namely: Group 1 was given acetaminophen1,33 mg/kgBW as a positive control/drug control. Group 2 was given *aqua pro injection* as a negative control/solvent control. Group 3 was given 1 dose of cucumber peel ethanol extract, which was 100 mg/kg BW. Group 4 was given 2 doses of cucumber peel ethanol extract, namely 200 mg/kg BW. Group 5 was given 3 doses of cucumber peel ethanol extract, namely 400 mg/kgBW. Group 6 was given 1 dose of cucumber peel methanol extract which was 100 mg/kg BW. Group 7 was given 2 dose of cucumber peel methanol extract which was 200 mg/kg BW. Group 8 was given 3 dose of cucumber peel methanol extract which was 400 mg/kg BW.

Result and Discussion

Cucumber peel is traditionally used to treat various diseases, one of which is fever. Cucumber peelcontains flavonoid, saponin, phenolic, steroid, protein, calcium compounds. Meanwhile, those that are efficacious as anti-fever drugs are flavonoid compounds. In this peptone induction method, it contains 5% as a fever inducer because the peptone injected into male white mice can stimulate the formation of fever. This peptone is injected subcutaneously. Antipyretic effectiveness of cucumber peel methanol and ethanol extract was determined by experiencing the rectal temperature of mice after administration of cucumber peel methanol extract compared to acetaminophen positive control.

Peptone 5% was given to the negative control group, positive control, test group at a dose of cucumber peel extract 100 mg/kg BW, 200 mg/kg BW and 400 mg/kg BW. The negative control in this study was distillate water. The positive control that was given acetaminophen was used to see the effect of fever medicine, while the test group was used to find out the effect of giving the extract to male mice induced by 5% peptone during the experiment. The dose of acetaminophen used was 1.64 mg/kg BW. Observation of rectal temperature in male mice for 180 minutes which started after 60 minutes of subcutaneous administration of 5% peptone so that it is easily absorbed in the mice's body as an antipyretic.

From the overall results of observations, it can be concluded that administration of methanol extract of cucumber peels to test animals induced by peptones can result in a decrease in temperature. This shows that in the cucumber peel there are compounds that can reduce temperature, the substances that play a role are flavonoids.

In knowing whether there was a significant difference in the observed data on temperature reduction between groups of methanol and ethanol extract of cucumber peels at doses of 100 mg/kg BW, 200 mg/kg BW, 400 mg/kg BW, positive control and negative control, ANOVA statistical analysis was performed *(One Way ANOVA)* using the SPSS program.

From the results of the ANOVA test calculation, it is known that the significant value is $p = 0.000$ ($p < 0.05$) this shows that there is a significant difference.

Table 1. Antipyretic Power Cucumber peel of Ethanol Extract

Time (minute)	Antipyretic Power of Test Compounds								
	T (°C)					% Antipyretic Power			
	Negative control	Acetaminophen	Dose Extract 100 mg/Kg WW	Dose Extract 200 mg/Kg WW	Dose Extract 400 mg/Kg WW	Acetaminophen	Dose Extract 100 mg/Kg WW	Dose Extract 200 mg/Kg WW	Dose Extract 400 mg/Kg WW
30	37.48	37.4	37.66	37.70	37.78	0.21	-0.48	-0.58	-0.80
60	37.44	37.2	37.58	37.48	37.40	0.64	-0.37	-0.10	0.10
90	37.36	37.02	37.42	37.24	37.12	0.91	-0.16	0.32	0.64
120	37.26	36.86	37.30	37.00	36.90	1.00	0.10	0.69	0.97
150	37.24	36.72	37.22	36.80	36.68	1.40	0.05	1.18	1.50
180	37.12	36.60	37.04	36.60	36.52	1.40	0.21	1.40	1.61
210	37.00	36.50	36.88	36.50	36.42	1.35	0.32	1.35	1.56
240	36.90	36.42	36.72	36.44	36.32	1.30	0.48	1.25	1.57

Table 2. Antipyretic Power Cucumber peel of Methanol Extract

Time (minute)	Antipyretic Power of Test Compounds							
	T(°C)				% Antipyretic Power			
	Acetaminophen	Dose Extract 100 mg/Kg WW	Dose Extract 200 mg/Kg WW	Dose Extract 400 mg/Kg WW	Acetaminophen	Dose Extract 100 mg/Kg WW	Dose Extract 200 mg/Kg WW	Dose Extract 400 mg/Kg WW
30	37.5	37.62	37.5	37.77	0.25	-0.57	-0.6	-0.6
60	37.3	37.59	37.45	37.56	0.66	-0.65	-0.16	0.2
90	37.1	37.48	37.24	37.16	0.91	-0.25	0.36	0.69
120	36.54	37.36	37.15	36.8	1.00	0.16	0.58	0.79
150	36.35	37.31	36.78	36.72	1.36	0.19	1.11	1.6
180	36.31	37.25	36.70	36.67	1.47	0.26	1.34	1.76
210	36.20	36.26	36.5	36.32	1.56	0.37	1.45	1.79
240	36.14	36.23	36.31	36.12	1.76	0.41	1.28	1.81

Antipyretic activity test of ethanol extract of cucumber peel (*Cucumis sativus* L.) to male white mice (*Mus musculus*) was started by subducting administration of 5% peptone/peptone induction. The effect of fever is stimulated by giving peptones which act as exogenous pyrogens to the body so that a mechanism for the formation of antibodies against germs occurs. When germs enter the body. the thermostat will react to increase body temperature to defend the body against germs. Fever can occur because of pyrogens being transported into the blood and associated with receptors in the anterior hypothalamic preoptic nucleus. so that prostaglandin levels increase and result in an increase in the hypothalamic set point.

Data on the results of the study showed that the ethanol extract of cucumber peel doses of 100 mg/kgB W. 200 mg/kg BW. 400 mg/kg BW. the negative control of aqua pro injection (water for injection). and the positive control of paracetamol both had antipyretic activity due to a decrease in temperature in each group of mice. There is a difference in the decrease in temperature at each dose given and the time of observation also affects the decrease in temperature in mice. The data can be seen in **Table 1** and **Table 2**.

In methanol extract with testing the same dose as ethanol. Namely 100 mg/kg BW. 200 mg/kg BW and 400 mg/kg BW. The Data are in accordance with **Table 2** showed significant data significance as seen from the decrease in temperature in the cucumber peel of methanol extract of mice.

Based on the results of the ANOVA test. the comparison of the negative control group treatment gave significant results in the comparison of the negative control group ($p = <0.05$) and the cucumber peel ethanol extract group at doses of 100 mg/kg BW. 200 mg/kg BW. 400 mg/kg BW ($p=<0.05$) which shows a difference. Therefore. it can be concluded that the dose of 100 mg/kg BW. 200 mg/kg BW. 400 mg/kghave effect to decrease the temperature. No toxic

effect has been observed from dose 100 to 400 mg/Kg BW**.** Another research show that the ethanol extract of papaya leaf with a dose of 100 mg / Kg BW, 200 mg / Kg BW, and 400 mg /Kg BW had antipyretic effect (Ningsih, 2018) and combination of extracts moringa leaves and bitter melon leaves also had antipyretic effect at the same dose (Wijaya, 2023)

Conclusion

Cucumber peel of Ethanol and Methanol extract (*Cucumis sativus L.)* at a dose of 100 mg/Kg BW. 200 mg/Kg BW and 400 mg/Kg BW each showed antipyretic activity so that they could provide antipyretic effects in mice and the effective dose Cucumber peel of Ethanol and Methanol extract *(Cucumis sativus L.)* used to reduce the rectal temperature of male white mice is at a dose of 400 mg/kg BW because the percentage of decreasing temperature is the greatest among the other dosage and to find the optimal dose that provides pharmacological effects.

Acknowledgements

Thanks to all people who have agreed to help this research journal so that it can be completed properly.

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