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Analgesic Activity of Ethanolic Corn Silk Extract (*Zea mays* L.)

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ABSTRACT

Zea mays Corn silk is an herbal plant that is used empirically to relieve pain. Corn silk is known to have alkaloid compounds (trigonelline and indole) and flavonoids (vitexine and apigenidine) that have potential analgesic effects. On the official website of Prediction of Activity Spectra for Substances (PASS), it is known that indole is useful as a cyclooxygenase and prostaglandin synthase inhibitor. This study aims to determine the analgesic activity of 70% Ethanolic corn silk (*Zea mays L*) extract using a rendal-selitto analgesimeter. The extract was evaluated at 125, 250, and 500 mg/kg BW. The positive control groups were treated with Mefenamic Acid 45 mg/kgBW, and CMC Na 0,5% suspension was given to negative control. All treatment administrations were performed orally. Pain threshold was evaluated with Ugo-Basil analgesimeter and analgesic activity was calculated with percent inhibition of analgesic. The percent pain inhibition of Ethanolic corn silk (*Zea mays L*) extract 125, 250 and 500 mg/kg BW were about 23.71%, 28.08%, and 33.83% compared to mefenamic acid 27,55%. The 500mg/kg BW of Ethanolic corn silk (*Zea mays L*) extract showed significant analgesic activity ($p<0.05$). In general, the data obtained from the present study elucidated that the extract possessed significant analgesic activities and recommended for further studies to determine the mechanism of action and toxicity.

Keywords: Zea mays L., corn silk, analgesic

Introduction

Pain is a conscious warning when tissue damage is occurring or about to occur (Sherwood, 2015). Based on data from an American study in 2012, there are 86.6 million adults who feel acute pain every day and 25.5 million feel chronic pain. Indonesia does not have research that addresses the prevalence of all types of pain yet (Kemenkes, 2022). However, 99% of healthcare professionals reported seeing a patient with pain as a chief complaint and acute pain as the most common complaint in Indonesian health services (Mardiyah et al., 2021).

Pain treatment uses synthetic analgesics such as non-opioids (NSAIDs) and opioids. NSAID analgesics can relieve pain by inhibiting the enzyme cyclooxygenase. The enzyme functions to metabolize arachidonic acid into prostaglandins. So, with the inhibition of the cyclooxygenase enzyme, prostaglandins are not formed, then pain will be reduced (Sartika, 2019). As for opioids, they can relieve pain by replacing the perception of pain with endorphin-like action, blocking the transmission of pain impulses, and increasing the pain threshold. Analgesics have several side effects including kidney damage, liver damage, hypersensitivity reactions, and most often can cause stomach irritation (Wardoyo & Oktarlina, 2019).

With these side effects, people are looking for alternatives to natural ingredients as a treatment. One of the natural materials that are easily obtained by the community and not utilized often is corn silk. The benefits of corn silk as an analgesic have not been fully explored. Some studies show that corn silk has compounds that can potentially inhibit pain. The compounds that have the potential to inhibit pain are flavonoids and alkaloids (Okokon et al., 2016). Based on Dr. Duke's Phytochemical and Ethnobotanical databases, it is known that corn silk has alkaloid compounds

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such as trigonelline and indole, besides that corn silk also has flavonoid compounds such as vitexin and apigenin. These compounds have potential analgesic effects (Dr. Duke, 2022). Based on PASS (Prediction of Activity Spectra for Substances), indole compounds have activity as prostaglandin synthase inhibitors dan cyclooxygenase inhibitors, while trigonelline has prostaglandin synthase inhibitor activity (PASS, 2022). These things are the reasons why researchers conduct analgesic test research on ethanol extract of corn silk.

Material and Methods

Research design, place, and time

The research was conducted at the Biomedical Laboratory, Faculty of Medicine, Islamic University of Malang (UNISMA), and UPT Laboratorium Herbal Materia Medika Batu. This research was conducted from February to May 2023 with Ethical approval from the Health Research Ethic Committee Faculty of Medicine, University of Islam Malang, Indonesia with approval ID number No.049/LE.001/X/03/2022 which is valid from October 25, 2022 to October 25, 2023.

Animals research

The criteria for the experimental animals used in this study are in Table 1.

Table 1. Research animal criteria

	NC	PC	D1	D2	D3
Age	6-8 weeks	6-8 weeks	6-8 weeks	6-8 weeks	6-8 weeks
Sex	Male	Male	Male	Male	Male
Body Weight	185.67± 15.424	180.33± 8.807	194.00± 8.165	186.00± 15.319	178.50± 14.350
Injury	-	-	-	-	-

Note: NC: negative control CMC Na 0.5%; PC: positive control mefenamic acid 45mg/kgBW; D1: Dose 1 (125mg/kgBW); D2: Dose 2 (250mg/kgBW); Dose 3 (500mg/kgBW).

Research materials

The Corn silk (*Zea mays* L.) powder was identified by UPT Laboratorium Herbal Materia Medika Batu with ID number 074/653/102.20-A/2022, 70% ethanol, Aquadest, chloroform, mefenamic acid, and CMC Na 0.5%, and phytochemical reagents from 'Merck' (NH3, FeCl3, HCl, H2SO4 2N, Meyer, Dragendorff, Ac_2O, H_2SO_4).

Preparation of ethanolic corn silk (Zea mays L.) extract

Ethanol extract of corn silk was made by kinetic-digestion maceration method by putting 500 grams of dry powder into an erlenmayer, dissolved with 70% ethanol as much as 20 times the weight of the powder (1:20) which is 10.000mL at 40^0C at 100rpm for 10 hours (Agustina et al., 2014). After that, the mixture was filtered using a Buchner funnel. Then evaporated using a rotary evaporator at a temperature of 50^0C and put into the oven at a temperature of 50^0C. Then it is suspended and administered orally into rats with a dose of 125mg/KgBW, 250mg/KgBW, and 500mg/KgBW (Chairunnisa et al., 2019).

Phytochemical screening

Phytochemical screening was carried out on the results of the maceration of corn hair (*Zea mays* L.) with ethanol solvent to determine the secondary metabolites present in the extract. 10 mL of corn silk extract was put into a separatory funnel filled with 40:40 chloroform:aquadest. Then shake and let stand until two layers are formed, namely the water phase (top) and the chloroform phase (bottom). The two layers are separated. The water phase is used to test flavonoids, phenols, and saponins. While the chloroform phase is used to test alkaloids, steroids, and terpenoids (Octaviani et al., 2019).

Analgesic activity assay

The rats were clamped on the paw and pressurized in grams with a certain weight and the rats would respond by pulling a leg or making a sound. Thirty minutes before the test, the control and the extract were administered orally, and then analgesic activity was examined for up to 240 minutes (Keswara & Handayani, 2019). The higher the AUC value obtained, the higher the analgesic effect produced (Yuandani et al., 2018).

Pain threshold is calculated with the trapezoidal formula and presented in the Area Under the Curve (AUC) then pain inhibition is calculated as a percentage (Purnomo & Tilaqza, 2022).

$$AUC_{n-1}^{n} = \frac{Ftn-1+Ftn}{2}(t_n - t_{n-1})$$

Note:
Ftn-1 = average load endurance at tn-1 (grams)
Ftn = average load endurance at tn (grams)
tn = 30 minutes later
tn-1 = 30 minutes previously

$$\%\text{pain inhibition} = \frac{B-A}{B} \times 100$$

Note:
A = AUC of pain threshold of negative control
B = AUC of pain threshold of treatment group (positive control, dose I, dose II, or dose III)

Statistical analysis

Data were tested for normality and homogeneity. If the distribution is normal and the data is homogeneous, then continue to the One-Way ANOVA statistical test and LSD test (Least Significance Different). Data analysis was conducted using Statistical Product and Service Solution (SPSS) 23rd version (Nur, 2018).

Results and Discussion

Phytochemical active substances of ethanolic corn silk (Zea mays L.) extract

In this study, phytochemical screening was carried out to determine the secondary metabolite compounds present in the results of ethanol maceration of corn silk (*Zea mays* L.). Phytochemical tests were carried out in three repetitions to get the results described in Table 2.

Table 2. Phytochemical screening of ethanolic corn silk (*Zea mays* L.) extract

Sample	First Repetition	Second Repetition	Third Repetition
Flavonoids	+	+	+
Saponins	-	-	-
Phenols	+	+	+
Alkaloids	+	+	+
Terpenoids	+	+	+

Note: (+) Positive; (-) Negative

Based on this phytochemical test on an ethanol extract of corn silk, it is proven to contain flavonoids, phenols, alkaloids, and terpenoids, but does not contain saponins. The results of this study are by the results of previous research phytochemical tests conducted by Abdiana (2017) which were shown to contain flavonoids, phenols, alkaloids, and terpenoids. Based on Dr. Duke, corn silk has saponin compounds, but this test did not prove the presence of saponins. This can be

caused by two things, such as temperature and length of extraction. In research conducted by Chairunnisa (2019), it is said that saponins will be absorbed at a temperature of 50^0C, and the extraction is carried out for 48 hours.

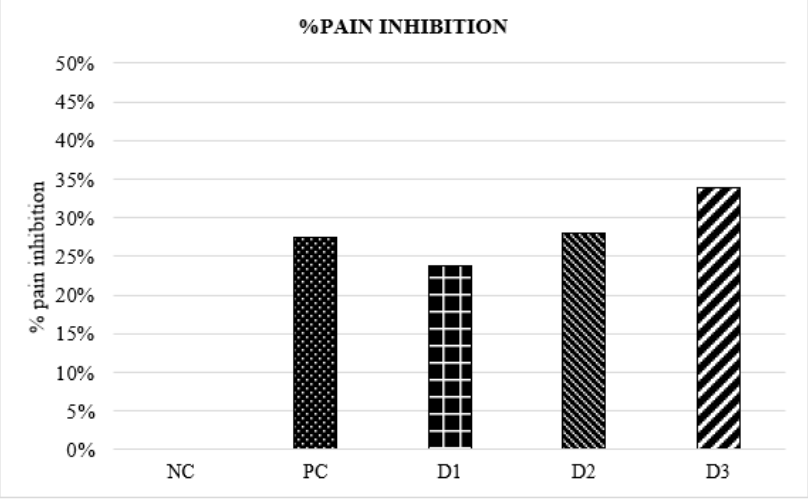
Analgesic effect of corn silk ethanolic extract

The results of the analgesic test of corn silk ethanol extract using the paw pressure test method on white rats can be seen from the AUC pain threshold in Table 3, and the percentage of pain inhibition in Figure 1.

Table 3. Deviation standard of AUC of pain threshold

Groups	AUC of Pain Threshold Data (Mean±SD)								
	30'	60'	90'	120'	150'	180'	210'	240'	AUC Total±SD
NC[a]	1845.83± 56.156	1785± 46.637	1727.5± 48.541	1702.5± 59.844	1672.5± 48.023	1627.5± 59.844	1595.0± 77.298	1610.0± 101.612	1695.73± 82.346
PC[b]	2020.83± 75.356	2167.5± 82.500	2285.0± 99.373	2377.5± 91.549	2480.0± 107.355	2545.0± 100.499	2467.5± 200.078	2380.0± 317.214	2340.42± 164.140
D1[b]	1946.67± 36.705	2122.5± 98.266	2255.0± 131.529	2360± 148.408	2392.5± 134.094	2337.5± 214.665	2242.5± 197.247	2125.0± 111.803	2222.71± 140.569
D2[b]	2020.00± 127.148	2175± 119.059	2330.0± 164.469	2442.5± 176.936	2515.0± 162.635	2500.0± 158.430	2470.0± 259.904	2410.0± 387.072	2357.81± 164.209
D3[c]	2200.00± 160.728	2400± 198.242	2562.5± 271.719	2687.5± 288.845	2775.0± 323.690	2812.5± 283.648	2675.0± 286.662	2387.5± 285.318	2562.50± 201.363

Note: NC: negative control CMC Na 0.5%; PC: positive control mefenamic acid 45mg/kgBW; D1: Dose 1 (125mg/kgBW); D2: Dose 2 (250mg/kgBW); Dose 3 (500mg/kgBW). a: statistically significant with positive control, dose I, dose II, and dose III; b: statistically equivalent; c: statistically significant with negative control, positive control, dose I, and dose II.



Note: NC: negative control CMC Na 0.5%; PC: positive control mefenamic acid 45mg/kgBW; D1: Dose 1 (125mg/kgBW); D2: Dose 2 (250mg/kgBW); Dose 3 (500mg/kgBW).

Figure 1. Histogram of pain inhibition percentage of ethanolic extract of corn silk

The ethanol extract has a significant difference from the negative control so the ethanol extract has an analgesic effect. The percentage of pain inhibition from the lowest to the highest is dose I, positive control, dose II, and dose III. Statistically also shows that Dose III has a significant difference to the positive control. which means that dose III is more effective in inhibiting pain than mefenamic acid. This can occur due to differences in the doses, the ethanolic extract of corn

silk dose I (125mg/kgBW), dose II (250mg/kgBW), dose III (500mg/kgBW), while the dose of mefenamic acid used was 45mg/kgBW [16]. The dose I is more than the positive control dose, but the percentage of pain inhibition of the positive control is higher than the dose I, that is because of the active substances of ethanolic corn silk extract dose I (125mg/kgBW) such as indole, trigonelline, and vitexin are less than others so that in inhibiting prostaglandins is not as effective as a positive control.

Based on Dr. Duke it is known that corn silk has alkaloids (trigonelline dan indole) and flavonoids (vitexin dan apigenin) compounds (Dr. Duke, 2022), same as research by Abdiana (2017). According to Prediction of Activity Spectra for Substances, indole compounds have prostaglandin synthase inhibitor and cyclooxygenase inhibitor activities, while trigonelline has activity as a prostaglandin synthase inhibitor (PASS, 2023). Cyclooxygenase is an enzyme that helps produce prostaglandins, and prostaglandins serve to activate nociceptors. If cyclooxygenase and prostaglandins are inhibited, then pain will be reduced (Silbernagl & Lang, 2016).

Conclusion

The weakness of this study is the toxic effects of the three doses are unknown. From this study, it can be concluded that:

1. Ethanol corn silk extract has an analgesic effect.
2. Etahol corn silk extract at doses of 125mg/KgBB and 250mg/KgBB in rats has an analgesic effect that is statistically equivalent to mefenamic acid 45mg/KgBB.
3. Ethanol corn silk extract dose 500mg/KgBB has a higher analgesic effect than mefenamic acid 45mg/KgBB.

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