



EVALUATION OF THE EFFECTIVENESS OF TURMERIC (CURCUMA LONGA LINN) METHANOL EXTRACT AS A PAIN RELIEVER AND FEVER REDUCER IN MALE WISTAR RATS

Chen Jiafei¹, Florenly²

¹Master of Clinical Medicine, Department of Clinical Medicine, Faculty of Medicine, Dentistry, Health Sciences, Universitas Prima Indonesia

²Department of Clinical Medicine, Faculty of Medicine, Dentistry, Health Sciences, Universitas Prima Indonesia

ABSTRACT

This study explores the potential of Turmeric (*Curcuma longa* Linn) as an antipyretic analgesic with flavonoid content in its methanol extract that can inhibit prostaglandins and reduce pain and fever. Although its use is still limited in Indonesia, this study aims to understand the analgesic and antipyretic effects of Turmeric methanol extract on male Wistar rats. The experimental design used the Post-Test Only Control Group to evaluate the antipyretic and analgesic effects at Prima Indonesia University Laboratory in January 2024. An acetic acid writhing test assessed an analgesic activity using a 0.7% acetic acid solution. The results showed the potential of Turmeric extract as an antipyretic and analgesic in male Wistar rats, especially at the highest dose (600 mg/kg body weight) after 5 hours of administration. The effect was more significant than the control and Standards groups, with hematological analysis showing increased extract dose. These findings support turmeric as a candidate for developing more effective antipyretic and analgesic drugs.

KEYWORDS: Turmeric (*Curcuma longa* Linn), Analgesic and antipyretic, Methanol extracts, Acetic acid writhing test, Analgesic and antipyretic effects

INTRODUCTION

Analgesics-antipyretics is a compound or drug used by humans of various ages to reduce pain and fever caused by multiple factors or conditions (Hung et al., 2018). This compound can relieve or eliminate painful sensations and reduce high body temperature due to fever. Therefore, analgesics-antipyretics are a common choice in treating symptoms such as headaches, muscle or joint pain, fever, and other conditions related to discomfort due to pain or elevated body temperature (Puspitaningrum et al., 2014). As such, analgesics-antipyretics are essential in human health care and well-being as they can help effectively manage bothersome symptoms (Puspitaningrum et al., 2014). Analgetics are compounds that can reduce or eliminate pain without removing consciousness.

Meanwhile, antipyretics can reduce fever (high body temperature) (Ponggele, 2013). A plant that can potentially act as an antipyretic analgesic compound is turmeric. Since ancient times, plants have been used in medicine and are still used today. In the beginning, trial and error methods were used to treat illnesses or even to feel better. The use of these plants has been gradually refined over generations, and these methods have become known in many contexts as traditional medicine (Cobra, 2019).

So many studies have been conducted to explore the various benefits of natural ingredients, one of which is Turmeric (*Curcuma longa* Linn). The methanol extract of Turmeric (*Curcuma longa* Linn) contains saponins, alkaloids, flavonoids, triterpenoids, tannins, and polyphenols (Helmalia, 2019).

Therefore, turmeric (*Curcuma longa* Linn) has various pharmacological effects, such as anti-inflammatory, antioxidant, antidiabetic, and antibacterial. Flavonoids in Turmeric (*Curcuma longa* Linn) can inhibit prostaglandins and have an antipyretic effect (Silalahi, 2018). The utilization of Turmeric (*Curcuma longa* Linn) for medicine in Indonesia is still not much, especially as an antipyretic analgesic. Thus, this study was designed to determine turmeric methanol extract's analgesic and antipyretic effects (*Curcuma longa* Linn) on male Wistar rats.

RESEARCH METHODS

This research is experimental research with Post-Test Only Control Group Design, which aims to explore the antipyretic and analgesic effects of Turmeric (*Curcuma longa* Linn). This research was conducted at Prima Indonesia University Laboratory in January 2024. The acetic acid writhing test method evaluated the analgesic activity of Turmeric (*Curcuma longa* Linn) extract. This method requires a 0.7% acetic acid solution, made using 0.7 ml of 100% glacial acetic acid dissolved in 100 ml of distilled water using a 100 ml volumetric flask. The preparation of this solution is done by first entering 20 ml of aquadest, then followed by 0.7 ml of 100% glacial acetic acid solution into a 100 ml volumetric flask, after which aquadest is added to the limit mark in a 100 ml volumetric flask.

Evaluation of the analgesic activity of this study was carried out using 25 rats grouped into five different groups:

- Control: Rats in this group were given 1 ml of 0.5% Na-CMC and, after 15 minutes, were injected 10 ml/kgBB of



- 0.7% acetic acid solution. After 5 minutes of injection, the number of writhing was counted in rats for 20 minutes.
- Standards (15 mg/kg body weight): Rats in this group were given an oral suspension of paracetamol 10 ml / kgBB. After 15 minutes, 10 ml / kgBB of 0.7% acetic acid solution was injected. After 5 minutes of injection, the number of writhing was counted in rats for 20 minutes.
 - Turmeric Extract (*Curcuma longa* Linn)-1 (200 mg/kg body weight): Rats in this group were given an oral suspension of Turmeric (*Curcuma longa* Linn) at a dose of 0.5 ml/kgBB and, after 15 minutes, were injected with 10 ml/kgBB of 0.7% acetic acid solution. After 5 minutes of injection, the number of writhing was counted in rats for 20 minutes.
 - Turmeric Extract (*Curcuma longa* Linn)-2 (400 mg/kg body weight): Rats in this group were given an oral suspension of Turmeric (*Curcuma longa* Linn) at a dose of 1 ml / kgBB and, after 15 minutes, were given an injection of 10 ml / kgBB of 0.7% acetic acid solution. After 5 minutes of injection, the number of writhing was counted in rats for 20 minutes.
 - Turmeric Extract (*Curcuma longa* Linn)-3 (600 mg kg body weight): Rats in this group were given an oral suspension of Turmeric (*Curcuma longa* Linn) at a dose of 1.5 ml/kgBB and, after 15 minutes, were injected with 10 ml/kgBB of 0.7% acetic acid solution. After 5 minutes of injection, the number of writhing was counted in rats for 20 minutes.
- Standards (600 mg kg body weight): Test animals were given an oral suspension of paracetamol 10 ml/ kgBB after 24 hours of induction. Food and drink were provided ad libitum.
 - Turmeric Extract (*Curcuma longa* Linn)-1 (200 mg/kg body weight): Test animals were given Turmeric extract (*Curcuma longa* Linn) at a dose of 0.5 ml / kgBB after 24 hours of induction. Food and drink were provided ad libitum.
 - Turmeric extract (*Curcuma longa* Linn)-2 (400 mg/kg body weight): Test animals were given Turmeric extract (*Curcuma longa* Linn) at a dose of 1 ml / kgBB after 24 hours of induction. Food and drink were provided ad libitum.
 - Turmeric extract (*Curcuma longa* Linn)-3 (600 mg kg body weight): Test animals were given Turmeric extract (*Curcuma longa* Linn) 1.5 ml / kgBB after 24 hours of induction. Food and drink were provided ad libitum.

The parameter measured to assess the analgesic activity of the sample is the number of writhes after 5 minutes of injection of 0.7% acetic acid solution for 20 minutes. In addition, the average inhibition of abdominal writhing can also be calculated by dividing the difference between the average number of writhes in the control group and the tested sample group by the average number of writhes in the control group multiplied by 100% (Saini & Singha, 2012).

Antipyretic activity testing in this study was carried out using the yeast-induced method. Brewer's Yeast solution was made from a 15% brewer yeast suspension form. The suspension dissolved 15 grams of brewer's yeast into 100 ml of normal saline. Then, 20 grams of the suspension was dissolved with 100 ml of distilled water to make a 20% brewer's yeast solution. This 20% brewer's yeast solution was induced by subcutis injection at 10 ml/kgBB. Before and 24 hours after induction, the rats' body temperature was measured rectally with a digital thermometer (Saini & Singha, 2012; Sivamurugan et al., 2016; Veronica et al., 2017).

Evaluation of antipyretic activity was carried out on 25 rats that had been induced by the Yeast-Induced method. The rats were then grouped into five groups, namely:

- Control: Test animals were given 1 ml of 0.5% Na CMC suspension after 24 hours of induction. Food and drink were provided ad libitum.

After being given turmeric methanol extract (*Curcuma longa* Linn), paracetamol was used as a standard, and Na-CMC was used as a control. Then, body temperature was measured every 1 hour for 5 hours after treatment. Then, the rats were dissected to take blood samples intracardiac using a three cc syringe with a 23 G needle. The blood samples obtained were then inserted into EDTA tubes. Before taking blood, the rats were anesthetized using chloroform. The EDTA blood samples were examined at the Health Laboratory, North Sumatra Provincial Health Office, for routine hematological examination (Maya and Chiuman, 2019; Chiuman, 2019).

The parameter in this study was the body temperature of rats measured by rectal body temperature measurement. The average percentage of decrease in body temperature of rats can be measured by sharing the difference between the average body temperature of rats 24 hours after induction and the average body temperature at a specific time after administration of the tested sample to the average body temperature of rats 24 hours after induction and multiplied by 100% (Saini and Singhal, 2012).

Data analysis in this study was carried out with IBM SPSS 25 software: phytochemical screening results, body weight of rats, number of writhing, and body temperature were analyzed by descriptive statistical analysis. Then, the analysis was continued with inferential statistical analysis according to the results of the data normality test using Shapiro-Wilk. If the data were normally distributed, parametric statistical analysis in the form of one-way ANOVA was performed, while if the data were not normally distributed, data transformation was performed. However, if the data is still abnormally distributed, an alternative test with non-parametric statistical analysis in Kruskal-Wallis is carried out.



RESEARCH RESULTS

Table 1. Data Normality Analysis with Shapiro-Wilk on Body Temperature Parameters

Parameters	Treatment Group	P-Value	Data Distribution
Body Temperature Before Induction	Control	0.146	Normal
	Standards	0.205	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -I	0.420	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -II	0.825	Normal
Body Temperature After Induction	Methanol Extract of Turmeric (Curcuma longa Linn) -III	0.150	Normal
	Control	0.925	Normal
	Standards	0.168	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -I	0.242	Normal
Body Temperature 1 Hour after Treatment	Methanol Extract of Turmeric (Curcuma longa Linn) -II	0.017	Abnormal
	Methanol Extract of Turmeric (Curcuma longa Linn) -III	0.012	Abnormal
	Control	0.496	Normal
	Standards	0.482	Normal
Body Temperature 2 Hours After Treatment	Methanol Extract of Turmeric (Curcuma longa Linn) -I	0.021	Abnormal
	Methanol Extract of Turmeric (Curcuma longa Linn) -II	0.112	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -III	0.582	Normal
	Control	0.481	Normal
Body Temperature 3 Hours After Treatment	Standards	0.495	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -I	0.191	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -II	0.561	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -III	0.251	Normal
Body Temperature 4 Hours After Treatment	Control	0.681	Normal
	Standards	0.658	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -I	0.616	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -II	0.182	Normal
Body Temperature 5 Hours After Treatment	Methanol Extract of Turmeric (Curcuma longa Linn) -III	0.847	Normal
	Control	0.492	Normal
	Standards	0.057	Abnormal
	Methanol Extract of Turmeric (Curcuma longa Linn) -I	0.941	Normal
Body Temperature 5 Hours After Treatment	Methanol Extract of Turmeric (Curcuma longa Linn) -II	0.252	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -III	0.688	Normal
	Control	0.185	Normal
	Standards	0.281	Normal
Body Temperature 5 Hours After Treatment	Methanol Extract of Turmeric (Curcuma longa Linn) -I	0.487	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -II	0.562	Normal
	Methanol Extract of Turmeric (Curcuma longa Linn) -III	0.829	Normal

The table above illustrates the results of statistical tests on body temperature before and after induction and body temperature several times after treatment with different treatment groups. All groups showed a normal data distribution in terms of body

temperature before induction. However, after induction, it was seen that some groups, such as Methanol Extract of Turmeric (Curcuma longa Linn) II and III, showed abnormal data distribution. When looking at body temperature several hours



after treatment, most groups showed normal data distribution, except for Methanol Extract of Turmeric (*Curcuma longa* Linn) I at 1 hour after treatment. In some groups, there were

significant differences in body temperature, indicated by p values less than the significance level of $p < 0.05$.

Table 2 Comparison of Body Temperature in All Treatment Groups

Treatment Group	Suhu Tubuh (°C)						
	Treatment Group	After induction**	1 Hours**	2 Hours*	4 Hours*	4 Hours*	5 Hours*
Control	45.34 ± 0.48	48.36 (0.40)	48.85 (1.40)	48.81 ± 0.11	48.12 ± 0.41	48.41 ± 0.14	48.01 ± 0.41 ^a
Standards	45.23 ± 0.28	48.21 (0.50)	48.50 (1.40)	48.41 ± 0.49	48.20 ± 0.21	48.02 ± 0.41	41.82 ± 0.22 ^{ab}
Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -I	45.12 ± 0.41	48.41 (0.50)	48.40 (0.90)	48.14 ± 0.42	48.44 ± 0.48	48.24 ± 0.40	41.90 ± 0.42 ^a
Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -II	45.44 ± 0.27	48.80 (0.40)	48.50 (0.80)	48.48 ± 0.11	48.00 ± 0.28	41.84 ± 0.24	41.10 ± 0.24 ^{ab}
Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -III	45.20 ± 0.17	48.23 (1.20)	48.10 (1.20)	48.18 ± 0.41	48.41 ± 0.41	41.81 ± 0.41	41.01 ± 0.14 ^b
P-value	0.881	0.527	0.284	0.912	0.102	0.152	0.014

Table 2 compares body temperature in all treatment groups over different periods. Body temperature was measured before, after, and at intervals of 1, 2, 4, and 5 hours after treatment. The treatment groups included a control, a standard group, and three groups that received Methanol Extract of Turmeric (*Curcuma longa* Linn) at various doses. Before induction, the average body temperature in the control group was 45.34°C, while the standard and treatment groups with turmeric methanol extract had values of 45.23°C and 45.12°C, respectively. After induction, body temperature increased in all groups, with the Control group reaching 48.36°C, the standard group reaching 48.21°C, and the treatment group with turmeric methanol extract varying from 48.41°C to 48.80°C. Further analysis was

carried out at certain time intervals. At 1 hour after treatment, all groups' body temperature increased significantly. However, there was no significant difference between the control, standard, and treatment groups. Furthermore, there were variations in body temperature between groups at intervals of 2, 4, and 5 Hours after treatment. The statistical analysis results showed no significant difference at 2 and 4 hours, but at 5 hours, there was a substantial difference between the groups. Thus, the results from this table show the comparison of body temperature between treatment groups over time, giving an idea of the potential body temperature effects of administering turmeric methanol extract in male Wistar rats.

Table 3 Data Normality Analysis with Shapiro-Wilk on the Parameter Number of Writhing

Parameters	Treatment Group	P-value	Data Distribution
Number of Wriggles	Control	0.854	Normal
	Standards	0.824	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -I	0.812	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -II	0.871	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -III	0.822	Normal

The normality analysis of writing data in the treatment groups, as listed in Table 4.8, using the Shapiro-Wilk test, showed that the distribution of data in all groups, including the control group, standard group, and the three treatment groups with Methanol Extract of Turmeric (*Curcuma longa* Linn), could be considered as a normal distribution. The p-values ranging from

0.812 to 0.871 indicated no significant difference in the normality of the data between groups. These results provide confidence that the data used in analyzing the number of wriggles met the assumption of normality, strengthening the validity of the statistical analysis performed on these parameters.

Table 4. Comparison of the Number of Writhing in All Treatment Groups

Treatment Group	Number of Writhing	P-Value
Control	10.51 ± 2.42 ^a	0.012
Standards	7.24 ± 2.42 ^{ab}	
Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -I	9.54 ± 2.64 ^a	
Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -II	7.53 ± 2.12 ^{ab}	
Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -III	2.23 ± 1.41 ^b	



Data are shown as Mean \pm SD. P values are obtained from One Way ANOVA analysis; different superscripts in the same column indicate significant differences.

Table 4. compares the number of writhing in all treatment groups. The One-way ANOVA analysis showed significant differences between groups with a value of $p=0.012$. The Control group showed a writhing count of 10.51 ± 2.42 , while the standard group had a writhing count of 7.24 ± 2.42 . The treatment group with Methanol Extract of Turmeric (*Curcuma*

longa Linn) showed variation, with group I having a writhing count of 9.54 ± 2.64 , group II of 7.53 ± 2.12 , and group III having the lowest writhing count, which was 2.23 ± 1.41 . Different superscripts in the same column indicate a significant difference between the groups. These results illustrate that turmeric methanol extract can potentially affect the amount of writhing in male Wistar rats, with substantial differences, especially in treatment group III, compared to the control and standard groups.

Table 5. Data Normality Analysis with Shapiro-Wilk on Hematology Parameters

Parameters	Treatment Group	P-value	Data Distribution
Hemoglobin (Hb)	Control	0.326	Normal
	Standards	0.477	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -I	0.743	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -II	0.344	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -III	0.475	Normal
Eritrosit (RBC)	Control	0.333	Normal
	Standards	0.033	Abnormal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -I	0.734	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -II	0.434	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -III	0.535	Normal
Leukosit (WBC)	Control	0.933	Normal
	Standards	0.734	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -I	0.337	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -II	0.333	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -III	0.530	Normal
Trombosit (PLT)	Control	0.555	Normal
	Standards	0.733	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -I	0.375	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -II	0.430	Normal
	Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -III	0.535	Normal

Table 5. displays the results of the normality analysis of hematological data using the Shapiro-Wilk test in the control, standard, and three treatment groups with Methanol Extract of Turmeric (*Curcuma longa* Linn). For hemoglobin (Hb), erythrocytes (RBC), leukocytes (WBC), and platelets (PLT) parameters, the distribution of data in the control, standard, and

all treatment groups can be considered as a normal distribution, except for the erythrocyte parameter in the standard group which shows abnormal distribution ($p=0.033$). These results provide a basis for the validity of hematological data in the analysis of treatment groups, strengthening the reliability of the interpretation of results on these parameters during this study.



Table 6. Comparison of Hematology Parameters in All Treatment Groups

Treatment Group	Hematologic			
	Hb* (gr/dL)	RBC** (x 20 ⁵ /μL)	WBC* (x 20 ³ /μL)	PLT* (x 20 ³ /μL)
Control	23.52 ± 3.25	7.59 (5.35)	7.72 ± 2.33 ^a	757.50 ± 323.23
Standards	23.02 ± 2.73	7.57 (3.95)	3.23 ± 2.02 ^b	550.53 ± 355.55
Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -I	23.32 ± 2.52	7.35 (3.50)	5.35 ± 0.55 ^a	700.52 ± 97.55
Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -II	23.07 ± 3.20	7.33 (5.30)	5.09 ± 0.27 ^c	757.30 ± 333.05
Methanol Extract of Turmeric (<i>Curcuma longa</i> Linn) -III	23.35 ± 0.55	7.25 (0.97)	3.32 ± 2.03 ^b	533.55 ± 333.22
P-value	0.531	0.462	0.014	0.531

*Data are shown as Mean ± SD. P values were obtained from A One-way ANOVA analysis; **Data are shown as median (range). P values were obtained from the Kruskal-Wallis analysis; a different superscript in the same column indicates significant differences.

Table 6 presents a comparison of hematological parameters, namely hemoglobin (Hb), erythrocytes (RBC), leukocytes (WBC), and platelets (PLT), in all treatment groups. The analysis results using One Way ANOVA showed significant differences in leukocyte count (WBC) parameters between groups (p=0.014). The control group had a hemoglobin value of 23.52 ± 3.25 gr/dL, erythrocyte count of 7.59 (5.35) x 10⁵/μL, leukocyte count of 7.72 ± 2.33 x 10³/μL, and platelet count of 757.50 ± 323.23 x 10³/μL. The standard group showed hemoglobin values of 23.02 ± 2.73 gr/dL, erythrocyte count of 7.57 (3.95) x 10⁵/μL, leukocyte count of 3.23 ± 2.02 x 10³/μL, and platelets of 550.53 ± 355.55 x 10³/μL. The three treatment groups with turmeric methanol extract had variations in the values of hematological parameters. Still, there was only a significant difference in the number of leukocytes (WBC) between treatment groups (p=0.014). Different superscripts in the same column indicate significant differences. These results provide an overview of the potential effect of turmeric methanol extract on hematological parameters, especially on leukocyte counts, in male Wistar rats.

DISCUSSION

The results showed that the methanol extract of turmeric (*Curcuma longa* Linn) can potentially be an antipyretic and analgesic. One hour after treatment, the control group showed a significant decrease in body temperature compared to the other treatment groups. At 2 Hours and 2 Hours after treatment, body temperature tended to approach the initial condition without significant differences between groups. It is important to note that the group receiving Methanol Extract of Turmeric (*Curcuma longa* Linn)-III showed a more substantial decrease in body temperature at some time after treatment compared to the control and standard groups. A p-value of less than 0.05 several times indicates a significant difference between groups, especially in the Methanol Extract of Turmeric (*Curcuma longa* Linn) -III group. Pain is an unpleasant subjective experience in one part of the body due to harmful stimuli. There are two types

of pain, namely neurogenic and peripheral pain. Peripheral pain is activated through stimulation of nociceptive afferent neurons, while neurogenic pain is activated by pain sensation through afferent input from pain sensation. The hot plate method is used to evaluate the analgesic effect of neurogenic pain, while intraperitoneal injection of acetic acid is used to assess the analgesic effect of peripheral pain. (Nitave, Chougule and Koumaravelou, 2017; Sharma *et al.*, 2020)

The pain sensation induced by acetic acid is a local inflammatory response caused by acetic acid injected into the peritoneum. This localized inflammation occurs through arachidonic acid metabolism from phospholipids in tissues via the cyclooxygenase (PGE2 and PGE2α) and lipooxygenase pathways. Thus, products of the cyclooxygenase pathway, such as PGE2 and PGE2α, and various products of the lipooxygenase pathway will be abundant in the peritoneal fluid. These products of the cyclooxygenase and lipooxygenase pathways cause swelling through cumulative permeability of the capillaries and the release of various endogenous mediators that will stimulate pain in the nerve endings of the nociceptors (Afsar *et al.*, 2015)

Fever is an increase in body temperature exhibited by various living things in response to the invasion of an infectious agent. Brewer yeast is a lipopolysaccharide (exogenous pyrogen), a component of gram-negative bacteria's cell wall. When pyrogens such as lipopolysaccharide (LPS) or brewer yeast enter the body, they damage the natural barrier. The brewer yeast then binds to an immunological protein called Lipopolysaccharide Binding Protein (LBP). This binding promotes the synthesis and release of various endogenous cytokines such as IL-1, IL-5, and TNFα. These endogenous cytokines easily cross the blood-brain barrier and act on the preoptic/ anterior hypothalamus, thus activating the arachidonic acid pathway and synthesizing and releasing prostaglandin E2. PGE2 is produced from the cyclooxygenase-2 pathway, causing an increase in body temperature (Santra *et al.*, 2012; Eldahshan and Abdel-Daim, 2015)

The antipyretic and analgesic effects of Turmeric (*Curcuma longa* Linn) are related to the presence of phenols and flavonoids in Turmeric (*Curcuma longa* Linn). Several studies



have reported the analgesic effects of alkaloids, phenols, and flavonoids. Flavonoids can inhibit the biosynthesis of prostaglandins involved in immunological responses and are also the end product of the cyclooxygenase and lipoxygenase pathways. Additionally, flavonoids also affect protein kinase, one of the regulatory enzymes that can inhibit inflammation (Eldahshan & Abdel-Daim, 2015). In addition to flavonoids, Gaichu et al. (2017) also reported that alkaloids, as phytochemical compounds, inhibit prostaglandin synthesis, which is one of the products of the cyclooxygenase pathway (Gaichu et al., 2017). Therefore, it can be concluded that the analgesic and antipyretic effects of Turmeric (*Curcuma longa* Linn) are due to alkaloids, phenols, and flavonoids. These phytochemical compounds inhibit prostaglandin biosynthesis, thereby preventing the cascade of inflammation and ultimately resulting in analgesic and antipyretic effects.

CONCLUSION

The study indicates that the Methanol Extract of Turmeric (*Curcuma longa* Linn) can act as an antipyretic and analgesic in male Wistar rats, especially at the highest dose (600 mg/kg body weight). The antipyretic and analgesic effects were observed after 5 hours of administration. The turmeric extract group showed a more significant decrease in body temperature than the control and standard groups, with hematological analysis results indicating a substantial reduction with increasing extract dose. These findings suggest that the Methanol Extract of Turmeric (*Curcuma longa* Linn) could be a candidate for further development as an antipyretic and analgesic drug.

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