International Journal of Multidisciplinary Research and Publications
ISSN (Online): 2581-6187

Test of the Activity of the Analgesic And Antipyretic Effects of Mangosteen Peel Methanol Extract (Garcinia Mangostana L.) Induction of Paracetamol in Male Wistar Rats

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Abstract**—** *Methanol extract of mangosteen peel (Garcinia mangostana L.) contains saponins, alkaloids, flavonoids, triterpenoids, tannins, and polyphenols. Flavonoids in mangosteen skin can inhibit prostaglandins so that they have an antipyretic effect. Based on the background description above, a problem can be formulated: "How is the analgesic and antipyretic effect of mangosteen fruit peel methanol extract (Garcinia mangostana L.) induced by paracetamol in white male rats Wistar strain? This type of research is experimental, with a Post-Test Only Control Group Design research design conducted from March 2022 until the end of June 2022. This research was conducted at the Pharmacy Laboratory of the University of North Sumatra Medan. The amount of yield obtained from mangosteen peel methanol extract is 7.52%. After 5 hours after treatment, the body temperature of rats experienced significant changes; this was reflected in the p-value <0.05 in the mangosteen peel methanol extract group (6.75 ± 0.42 x 106 / µL) and the control group (8.31 ± 1.14 x 106 / µL) there was no significant difference in the number of leukocytes. The conclusion is that mangosteen peel methanol extract contains various phytochemicals: Alkaloids, Saponins, Flavonoids, Tannins, and Steroid Terpenoids. Methanol extract from mangosteen skin has a significant antipyretic effect (p-value ≤ 0.05) after 5 hours of administration at the optimal 750 mg/kg BW dose. Methanol extract from mangosteen peel has an analgesic effect on nociceptive pain at an optimal amount of 500-750 mg/kg body weight.*

Keywords**—** *Mangosteen, Methanol, antipyretic, analgesic*.

I. INTRODUCTION

Analgesics-antipyretics are compounds that people of all ages often use to reduce pain and fever for various reasons. Analgesics are compounds that can reduce or eliminate pain without losing consciousness. At the same time, antipyretics can reduce fever (high body temperature). Plants that can potentially be antipyretic analgesic compounds are mangosteen fruit (Garcinia mangostana L) (1). Methanol extract of mangosteen fruit peel (Garcinia mangostana L.) contains saponins, alkaloids, flavonoids, triterpenoids, tannins, and polyphenols (2). Therefore, mangosteen peels have various pharmacological effects such as anti-inflammatory, antioxidant, antidiabetic, and antibacterial (3); (1); (4). In addition, flavonoids in mangosteen skin can inhibit prostaglandins so that they have an antipyretic effect (Suwertayasa, 2013). Based on the background description above, a problem can be formulated as "How is the analgesic and antipyretic effect of methanol extract of mangosteen rind (Garcinia mangostana L.) induced by paracetamol in Wistar male white rats?

II. LITERATURE REVIEW

The main phytochemicals in this species are terisoprenylated xanthones, a class of secondary metabolites with many reports on biological effects, such as antioxidant, pro-apoptosis, anti-proliferation, antinociceptive, anti-inflammatory, neuroprotective, hypoglycemic, and anti-obesity. According to research by Pasaribu et al. (2012), 96% of ethanol extract of mangosteen fruit peel contains chemical compounds of alkaloid, flavonoid, glycoside, saponin, tannin, and steroid/triterpenoid groups (5). Antipyretic analgesics are compounds that can relieve pain and can reduce fever. Therefore, mangosteen peel's flavonoid and alkaloid content can provide analgesic effects. In addition, flavonoids can inhibit prostaglandins so that they have an antipyretic effect (6).

III. RESEARCH METHODS

This type of research is experimental, with a Post-Test Only Control Group Design research design carried out from March 2022 until the end of June 2022. This research was conducted at the Pharmacy Laboratory of the University of North Sumatra, Medan.

Tools, materials, and experimental animals

EDTA tube, five cc syringe, three cc syringe, one cc syringe, digital thermometer, 100 ml measuring flask, 10 ml measuring flask, filter paper, shell paper, analytical scales, blender, macerator vessel, rotary evaporator, test tube, improved Neubauer counting chamber, and hemometer. Methanol, Brewer yeast, Normal Saline, Chloroform, NA-CMC, Paracetamol, Mangosteen Peel, Glacial Acetic Acid, Aquadest, FeCl3, HCl, Amyl Alcohol, Sulfuric Acid, Magnesium Powder, Zinc Powder, Ammonia.

Preparation of Mangosteen peel Ethanol Extract Test Ingredients

Mangosteen peels Simplicia weighed as much as 200 grams each, then extracted using a maceration technique with 400 ml of 98% methanol solvent. Maceration is carried out for one week with occasional stirring regularly. The filtrate is then

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evaporated using a rotary vacuum evaporator with a temperature of 50oC until a paste-shaped extract is obtained and stored at 20oC (Vasanthakumar D et al., 2015). In phytochemical test studies using fans-worth method modifications, we identify phenols, steroids/triterpenoids, terpenoids, saponins, flavonoids, tannins, and alkaloids.

Na CMC Suspension Making 0.5%

A total of 0.5 grams of Na CMC is sprinkled into a mortar containing 10 mL of hot distilled water. It is allowed to stand for 15 minutes until a transparent period is obtained, ground until a gel forms, diluted with a small amount of distilled water, then poured into a 100 mL flask, and filtered water to the limit of the mark. This suspension is used as an extract carrier and rutin.

Suspension mangosteen Peel Extract

A total of 1 gram of mangosteen peel extract is put into a mortar, and a 0.5% Na CMC suspension is added little by little while grinding until homogeneous and then put into a 10 mL flask. Volume is sufficient with 0.5% Na CMC suspension up to the marking line.

Paracetamol Suspension Manufacturing

150 mg of paracetamol was ground into a mortar; then, a 0.5% Na CMC suspension was added and put into a 10 mL flask. Volume is sufficient with 0.5% Na CMC suspension up to the marking line.

Analgesic Activity Testing

Evaluation of the analgesic activity of mangosteen peel extract was carried out by the acetic acid writhing test method. This method requires a 0.7 % acetic acid solution prepared using 0.7 ml of 100% glacial acetic acid dissolved in 100 ml aqua dest through a 100 ml measuring flask. The manufacture of this solution is carried out by first entering aqua dest as much as 20 ml, then followed by 0.7 ml of 100% glacial acetic acid solution into a 100 ml measuring flask, after which aqua dest is added up to the limit mark on the 100 ml measuring flask.

Evaluation of analgesic activity from this study was carried out using 25 mice grouped in 5 different groups:

a. Control: Rats in this group were given 1 ml of 0.5% Na-CMC and, after 15 minutes, was given an injection of 10 ml/kg body weight of 0.7% acetic acid solution. After 5 minutes of injection, the amount of writhing in mice was calculated for 20 minutes.
b. Standard (150 mg/kg body weight): Rats in this group were given an oral suspension of paracetamol 10 ml/ kg body weight. After 15 minutes were given an injection of 10 ml/kg body weight of 0.7% acetic acid solution. After 5 minutes of injection, the amount of writhing in mice was calculated for 20 minutes.
c. Mangosteen Peel Extract-1 (250 mg/kg body weight): Rats in this group were given an oral suspension of mangosteen peel at a dose of 2.5 ml/kg body weight and, after 15 minutes, were given an injection of 10 ml/kg body weight of a 0.7% acetic acid solution. After 5 minutes of injection, the amount of writhing in mice was calculated for 20 minutes.
d. Mangosteen Peel Extract-2 (500 mg/kg body weight): Rats in this group were given an oral suspension of Mangosteen Peel at a dose of 5 ml/kg body weight and, after 15 minutes, were given an injection of 10 ml/kg body weight of 0.7% acetic acid solution. After 5 minutes of injection, the amount of writhing in mice was calculated for 20 minutes.
e. Mangosteen Peel Extract-3 (750 mg/kg body weight): Rats in this group were given an oral suspension of mangosteen peel at a dose of 7.5 ml/kg body weight and, after 15 minutes, were given an injection of 10 ml/kg body weight of a 0.7% acetic acid solution. After 5 minutes of injection, the amount of writhing in mice was calculated for 20 minutes.

The measured parameter for assessing the analgesic activity of the sample was the amount of writing after 5 minutes of injection of a 0.7% acetic acid solution for 20 minutes. In addition, it can also be calculated the average inhibition of abdominal writhing by sharing the difference between the average number of writhings in the control group and the sample group tested against the average number of writhings in the control group multiplied by 100% (7–9).

Antipyretic Activity Testing

Testing of antipyretic activity in this study was carried out by the Yeast-Induced method. Brewer's Yeast solution is prepared from the form of a 15% brewer yeast suspension. The suspension is made dissolving 15 grams of brewer's yeast into 100 ml of normal saline. Then, 20 grams of the suspension is then dissolved with 100 ml of aquadest to make a 20% brewer's yeast solution. This 20% brewer's yeast solution is induced by subcutaneous injection at a dose of 10 ml/kg body weight. Before and 24 hours after induction, rat body temperature was measured rectally with a digital thermometer (7–9).

Evaluation of this antipyretic activity was carried out on 25 rats that had been induced by the Yeast-Induced method. These mice were then grouped into 5 groups, namely:

a) Control: Test animals were given 1 ml of 0.5% Na CMC suspension after 24 hours of induction. Food and drinks are given ad libitum.
b) Standard (150 mg/kg body weight): Test animals were given oral suspension of paracetamol 10 ml/ kg body weight after 24 hours of induction. Food and drinks are given ad libitum.
c) Mangosteen Peel Extract-1 (250 mg/kg body weight): The test animal was given mangosteen peel extract at a dose of 2.5 ml/ kg body weight after 24 hours of induction. Food and drinks are given ad libitum.
d) Mangosteen Peel Extract-2 (500 mg/kg body weight): The test animal was given mangosteen peel extract at a dose of 5 ml/ kg body weight after 24 hours of induction. Food and drinks are given ad libitum.
e) Mangosteen Peel Extract-3 (750 mg/kg body weight): The test animal was given Mangosteen Peel extract of 7.5 ml/ kg body weight after 24 hours of induction. Food and drinks are given ad libitum.

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After being given methanol extract of mangosteen peel, paracetamol as standard, and Na-CMC as control. Thus, body temperature measurements are carried out once every 1 hour for 5 hours after treatment. Then, the mice were dissected to take blood samples intracardially using a 3 cc syringe with a needle measuring 23 G. Blood samples obtained were then inserted into an EDTA tube. Before taking the blood of rats, it is dianastesied using chloroform. The EDTA blood sample was examined at the Health Laboratory, North Sumatra Provincial Health Office for routine hematology examination (10).

The parameters measured in this study were rat body temperatures which were measured by rectal body temperature measurements. The average percentage of rat body temperature drops can be measured by sharing the difference between the average body temperature of mice 24 hours after induction and the average body temperature at a specific time after the administration of samples tested against the average body temperature of mice 24 hours after induction and multiplied by 100% (7–9).

Data Analysis

The data were analyzed using the Shapiro-Wilk method to see the normality of the data. If the data is normally distributed (P > 0.05), proceed using the One Way ANOVA method to determine the average difference between the groups. If there is a difference, (P < 0.05) followed by the Post Hoc Tukey HSD test to see the real difference between treatments. But if the distributed data is abnormal then the Kruskal-Wallis test is used

IV. Result and Discussion

TABLE 1. Characteristics of Mangosteen Bark Methanol Extract (Garcinia Mangostana L)

Characteristic	Value
Weight of Fresh Simplisia (gr)	500 gr
Weight of Dry Simplisia Powder (gr)	212 gr
Solvent Volume (ml)	2120 ml
Extract Weight (gr)	16,20 gr
Amendment (%)	7.52%

From the data of the table above, it can be seen that from 500 gr of mangosteen peel samples, an extract of 16.20 grams was found. Thus, the amount of yield obtained from mangosteen peel methanol extract is 7.52%.

TABLE 2. Phytochemical Screening Results of Mangosteen Skin Methanol Extract

Phytochemicals	Reagents	Results
Alkaloids	Bouchardart	+
	Mayer	+
	Dragondroff	-
	Wagner	+
Saponins	Aquadest + Alcohol 96%	-
Flavonoids	FeCl3 5%	+
	$Mg_{(s)} + HCl_{(p)}$	-
	NaOH 10%	-
	$H_2SO_{4\ (p)}$	-
Tanin	$FeCl_3$ 1%	+
Steroids and Terpenoids	Salkowsky	-
	Liberman Bouchard	+

From the table data above, it can be seen that mangosteen peel methanol extract contains several phytochemical compounds including Alkaloids, Saponins, Flavonoids, Tannins, as well as Steroids and Terpenoids.

Antipyretic Effects

In evaluating the antipyretic effect of mangosteen bark methanol extract, body temperature measurements were taken in 7 different observation times, namely: before induction, after induction (24 hours), 1 hour, 2 hours, 3 hours, 4 hours, and 5 after treatment. All of these parameters are then analyzed for normality with Shapiro-wilk and the results of the analysis can be seen in the following table:

TABLE 3. Data Normality Analysis with Shapiro-Wilk on Body Temperature Parameters

Parameters	Treatment Groups	*p-value*	Data Distribution
Body Temperature Before Induction	Control	0.134	Usual
	Standard	0.204	Usual
	Mangosteen Bark Methanol Extract -I	0.331	Usual
	Mangosteen Bark Methanol Extract -II	0.745	Usual
	Mangosteen Bark Methanol Extract -III	0.110	Usual
Body Temperature After Induction	Control	0.966	Usual
	Standard	0.170	Usual
	Mangosteen Bark Methanol Extract -I	0.237	Usual
	Mangosteen Bark Methanol Extract -II	0.011	Abnormal
	Mangosteen Bark Methanol Extract -III	0.011	Abnormal
Body Temperature 1 Hour after Treatment	Control	0.394	Usual
	Standard	0.376	Usual
	Mangosteen Bark Methanol Extract -I	0.027	Abnormal
	Mangosteen Bark Methanol Extract -II	0.111	Usual
	Mangosteen Bark Methanol Extract -III	0.574	Usual
Body Temperature 2 Hours after Treatment	Control	0.472	Usual
	Standard	0.491	Usual
	Mangosteen Bark Methanol Extract -I	0.196	Usual
	Mangosteen Bark Methanol Extract -II	0.569	Usual
	Mangosteen Bark Methanol Extract -III	0.254	Usual
Body Temperature 3 Hours after Treatment	Control	0.678	Usual
	Standard	0.658	Usual
	Mangosteen Bark Methanol Extract -I	0.613	Usual
	Mangosteen Bark Methanol Extract -II	0.175	Usual
	Mangosteen Bark Methanol Extract -III	0.743	Usual
Body Temperature 4 Hours after Treatment	Control	0.391	Usual
	Standard	0.052	Usual
	Mangosteen Bark Methanol Extract -I	0.940	Usual
	Mangosteen Bark Methanol Extract -II	0.256	Usual
	Mangosteen Bark Methanol Extract -III	0.685	Usual
Body Temperature 5	Control	0.174	Usual
	Standard	0.271	Usual

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Parameters	Treatment Groups	*p-value*	Data Distribution
Hours after Treatment	Mangosteen Bark Methanol Extract -I	0.481	Usual
	Mangosteen Bark Methanol Extract -II	0.564	Usual
	Mangosteen Bark Methanol Extract -III	0.823	Usual

From the table data above, it can be seen that the body temperature data 24 hours after induction and 1 hour after the distributed treatment are abnormal. While the body temperature before induction and 2-5 hours after induction of normally distributed treatment. Based on the distribution of these data, a comparison of body temperature was carried out during the study in all treatment groups. The results of the comparison are shown in the following table.

TABLE 4. Comparison of Body Temperature across Treatment Groups

Treatment Groups	Suhu Tubuh (ºC)						
	Before Induction *	After Induction **	1 Hour **	2 Hour *	3 Hour *	4 Hour *	5 Hour *
Control	36.30 ± 0.37	38.11 (0.40)	37.70 (1.40)	37.72 ± 0.61	37.62 ± 0.46	37.36 ± 0.63	37.05 ± 0.45[a]
Standard	36.32 ± 0.27	38.00 (0.50)	37.60 (1.40)	37.46 ± 0.49	37.20 ± 0.26	37.02 ± 0.46	36.72 ± 0.22[ab]
Mangosteen Bark Methanol Extract -I	36.18 ± 0.31	38.30 (0.50)	38.20 (0.90)	37.64 ± 0.42	37.34 ± 0.38	37.24 ± 0.30	36.90 ± 0.32[a]
Mangosteen Bark Methanol Extract -II	36.34 ± 0.21	37.80 (0.40)	37.60 (0.80)	37.48 ± 0.61	37.00 ± 0.28	36.84 ± 0.23	36.60 ± 0.24[ab]
Mangosteen Bark Methanol Extract -III	36.20 ± 0.19	38.00 (1.20)	38.10 (1.20)	37.58 ± 0.36	37.36 ± 0.46	36.86 ± 0.36	36.14 ± 0.12[b]
Nilai P	**0.978**	**0.181**	**0.281**	**0.917**	**0.104**	**0.167**	**0.001**

*The data is displayed as Mean ± SD. The *p-value* is obtained from the One Way ANOVA analysis; **Data is displayed as Median (Range). The *p-value* is obtained from kruskal-wallis analysis; Different superscripts in the same column show significant differences.

From the data of the table above it can be seen that, the entire body temperature of mice at the time before induction was uniform, this is reflected in the Value of P> 0.05 (*p-value* = 0.978). After 24 hours of induction, the rat's body temperature remained uniform, this can be seen from the *p-value* > 0.05 (*p-value* = 0.181). However, the body temperature of rats after induction of cendeurng increased compared to before induction. Before induction the body temperature of rats had a tendency between 36.24-36.34ºC and increased with a range of 37.90-38.30ºC after 24 hours of induction.

After 24 hours of induction, the entire group of mice was given treatment according to their treatment group. The body temperature of the rats 1-4 hours after treatment did not show significant differences between the treatment groups. This can be seen from the *p-value* of the rat's body temperature every hour which is greater than 0.05. However, at the end of the observation, which was 5 hours after treatment, the rat's body temperature underwent a significant change, this was reflected in the *p-value* < 0.05 (*p-value* = 0.001). Where, the mangosteen peel methanol extract group III showed the lowest body temperature 5 hours after treatment, namely 36.14 ± 0.12 ºC and the Mangosteen Peel methanol extract group -III also showed a significant difference to the control group which showed the highest body temperature of 37.36 ± 0.46 ºC.

Analgesic Effects

In evaluating the analgesic effect of mangosteen bark methanol extract, a calculation of the amount of writhing was carried out on the entire rat treatment group after being injected with acetic acid. Then, this parameter is analyzed for normality with Shapiro-wilk and the results of the analysis can be seen in the following table.

TABLE 5. Data Normality Analysis with Shapirwo-Wilk on Writhing Parameters

Parameters	Treatment Groups	P-value	Data Distribution
Amount of Activity	Control	0.926	Usual
	Standard	0.201	Usual
	Mangosteen Peel Methanol Extract -I	0.331	Usual
	Mangosteen Peel Methanol Extract -II	0.615	Usual
	Mangosteen Peel Methanol Extract -III	0.927	Usual

From the data of table 5 it can be seen that the value of P > 0.05. This indicates that the distributed data is normal. Based on the normality of these data, a comparison of the number of mice was carried out in all groups of mice. From the data of table 6. it can be seen that the *p-value* < 0.05 (*p-value* = 0.002). This shows that there are significant differences in the amount of activity between the treatment groups. The least amount of geliat found in the mangosteen-III bark methanol extract group was 5.22 ± 1.91 and this number showed significant differences with the mangosteen peel methanol extract group -I (12.81 ± 3.12) and the control group (11.10 ± 1.91). The results of the comparison of the number of geliat in the entire group of mice can be seen in the following table.

TABLE 6. Comparison of Writhing In All Treatment Groups

Treatment Groups	Amount of Activity (*Writhing*)	P-Value
Control	11.10 ± 1.91[a]	0.002
Standard	8.82 ± 3.26[ab]	
Mangosteen Peel Methanol Extract -I	12.81 ± 3.12[a]	
Mangosteen Peel Methanol Extract -II	8.83 ± 3.36[ab]	
Mangosteen Peel Methanol Extract -III	5.22 ± 1.91[b]	

The data is displayed as Mean ± SD. The *p-value* is obtained from the Way ANOVA analysis; Different superscripts in the same column show significant differences.

The data in the table below shows that neither hemoglobin levels, erythrocyte count, nor platelet count showed significant differences between treatment groups. The range of hemoglobin, erythrocyte, and platelet counts in the entire group of mice was 12.10-14.22 gr/dL, 7.02-7.23 x 106/µL, and 624.65-867.40 x 103/µL. Only the number of leukocytes showed a significant difference between the treatment groups, reflected in the *p-value* of < 0.05. The standard group (3.06 ± 1.01 x 106/µL) and mangosteen peel methanol extract (3.35 ± 1.07 x 106/µL) showed significant differences from other

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treatment groups. The group with the most leukocytes was the control group, followed by the Mangosteen Bark methanol extract groups-I, II, III, and standard. However, in the Mangosteen Peel methanol extract group (6.75 ± 0.42 x 106/μL) and the control group (8.31 ± 1.14 x 106/μL), there was no significant difference in the number of leukocytes.

TABLE 7. Comparison of Hematology Parameters across Treatment Groups

Treatment Groups	Hematologic			
	Hb* (gr/dL)	RBC** (x 10^6/μL)	WBC* (x 10^3/μL)	PLT* (x 10^3/μL)
Control	14.53 ± 4.02	7.64 (6.35)	8.31 ± 1.14[a]	867.60 ± 214.14
Standard	14.01 ± 1.85	7.67 (2.95)	3.06 ± 1.01[b]	650.62 ± 366.56
Mangosteen Peel Methanol Extract -I	12.10 ± 1.32	7.25 (2.60)	6.75 ± 0.42 [a]	800.61 ± 97.55
Mangosteen Peel Methanol Extract -II	14.22 ± 3.19	7.23 (5.20)	5.09 ± 0.1 7[c]	867.40 ± 423.06
Mangosteen Peel Methanol Extract -III	12.92 ± 0.60	7.02 (0.98)	3.35 ± 1.07[b]	624.65 ± 242.11
P-Value	**0.649**	**0.512**	**0.05**	**0.523**

*Data are shown as Mean ± SD. *P-value* s obtained from One Way ANOVA analysis; **Data are shown as Median (Range). *P-value* s obtained from Kruskal-Wallis analysis; Different superscript in the same column indicates significant difference.

The results of this study show that mangosteen peel has a potential antipyretic and analgesic effect. This suggests that mangosteen peel in the form of methanol extract obtained by maceration has an antipyretic effect after 5 hours of administration of the section. Antipyretic effects were mainly observed at the two highest doses of 500 mg/kg body weight and 750 mg/kg body weight. However, the analgesic effect of mangosteen peel is found at the highest dose of 750 mg/kg body weight. Meanwhile, hematologic examination results showed a significant decrease in line with the increase in the mangosteen peel methanol extract. Pain is an unpleasant subjective experience in one part of the body as a result of harmful stimuli. There are different types of pain, namely neurogenic and peripheral pain. Peripheral pain is activated through excitation in the nociceptive afferent neurone whereas neurogenic pain is activated by pain sensai through the afferent input of the pain sensation. To evaluate the analgesic effect of neurogenic pain was done through the hot plate method while intraperitoneal injection of acetic acid was performed to evaluate the analgesic effect of peripheral pain (11). The products of this cyclooxygenase and lipoxygenase pathways that cause swelling through cumulative permeability in the capillaries and the release of various endogenous mediators that will stimulate pain in the nerve endings of nosirsceptors (12).

When pyrogens such as lipopolysaccharides (LPS) or brewer yeast enter the body by damaging the natural barrier. This yeast then binds to an immunological protein called Lipopolusaccharide Binding Protein (LBP). This binding promotes the synthesis and release of various endogenous cytokines such as IL-1, IL-6, TNFα. These endogenous cytokines easily cross the blood brain barrier and act on the preoptic/ anterior hypothalamus, thus activating the arachidonic acid pathway resulting in the synthesis and release of prostaglandin E2. PGE2 is produced from the cyclooxygenase-2 pathway, causing a rise in body temperature (13). The anapyretic and analgesic effects of mangosteen peel are related to the content of phenols and flavonoids present in mangosteen peel. Various studies have reported analgesic effects possessed by alkaloid compounds, phenols, and flavonoids. Flavonoids can inhibit prostaglandin biosynthesis involved in the immunological response and are also the end products of the cyclooxygenase and lipoxygenase pathways.

Gaichu et al. (2017) also report that alkaloid compounds as phytochemical compounds also inhibit the synthesis of prostaglandins which are one of the products of the cyclooxygenase pathway (14). So it can be concluded that the analgesic and antipyretic effects of Mangosteen Peel are caused due to the presence of alkaloids, phenols, and flavonoids. These phytochemical compounds will inhibit the biosynthesis of prostaglandins, thus preventing cascade inflammation, and will eventually produce analgesic and antipyretic effects. This study's results were supported by research (1), which stated that mangosteen peel ethanol extract (Garcinia mangostana L) was proven to have an antipyretic analgesic effect with an effective dose of 50 mg/kg of rat body weight. Furthermore, research (1) states that mangosteen peel extract has an analgesic effect that begins to be seen at the 30th minute to the 120th minute, with the maximum effect seen at the 90th minute, with a concentration of 10%.

V. CONCLUSION

Based on the results of research, observations and discussions, it can be concluded that mangosteen peel methanol extract contains various phytochemicals, namely Alkaloids, Saponins, Flavonoids, Tannins, as well as Steroids and Terpenoids. Mangosteen bark methanol extract has a significant antipyretic effect (*p-value* ≤ 0.05) after 5 hours of administration at an optimal dose of 750 mg/kg body weight. Mangosteen Bark methanol extract has an analgesic effect against nociceptive pain at an optimal dose of 500-750 mg/kg body weight.

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