

## THE EFFECT OF GIVING KATE MAS LEAF EXTRACT (*Euphorbia heterophylla* L.) AS LAXATIVE ON MICE (*Mus musculus*)

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### ABSTRACT

Kate Mas plant (*Euphorbia heterophylla*) is a weed plant that grows in humid areas. Traditionally kate mas leaves are used to treat constipation, bronchitis, anti-inflammatory and asthma. The purpose of this study was to determine the effect of giving kate mas leaf extract (*Euphorbia heterophylla*) as a laxative to mice (*Mus musculus*). The research design was experimental at the Pharmacology Laboratory, Faculty of Mathematics and Natural Sciences, Pancasakti University. This study used 15 mice which were divided into 5 groups which had been fasted 1 hour before treatment, using loperamide HCl suspension as inducer. The first group was given CMC Na suspension as a negative control, the second group was given dulcolactol syrup as a positive control, groups three, four and five as the treatment group were given katemas leaf ethanol extract with doses of 70 mg/20 g BW, 140 mg/20 g BW and 280 g respectively. mg/20g BW. Data were analyzed using the SPSS application, the Kruskal-Wallis Test followed by testing using the Mann-Whitney Test method to see differences between treatment groups. The results showed that kate mas leaf extract had a laxative effect on mice. The first dose treatment group, namely 70 mg/20 g BW, had the same laxative effect as the positive control group with a significance value ( $P > 0.05$ ) from these results it could be concluded that kate mas leaf extract had a laxative effect on mice, the most effective treatment group was group three with a dose of 70 mg/20 g BW.

**Keywords:** kate mas, laxative, constipation, mice.

### INTRODUCTION

Constipation is a health problem that often occurs and can have serious consequences if not treated immediately. Constipation is often found in society, generally caused by a lack of consumption of foods containing fiber, not drinking enough water and not moving enough. Based on the pathophysiology, constipation can be classified into constipation due to structural abnormalities and functional constipation. Constipation due to structural abnormalities occurs through obstruction of fecal flow, while functional constipation is related to colonic or anorectal motility disorders (Sembiring, 2017).

The average prevalence of constipation complaints in adult patients throughout the world is 16%, while in pediatric patients it is 12%. A systematic review reported that the prevalence of constipation increased at the age of 60-110 years, namely 35.5% and was higher in women. The prevalence of constipation in Asian communities such as Hong Kong, China, Korea and India varies between 8.2% to 16.8%. The epidemiology of constipation in Indonesia is 10.2%. A study in Jakarta in 1998-2005, reported that of 2,397 colonoscopies, 9% of them were carried out for indications of constipation, where there were more women than men (Abyan, dkk 2021).

In pharmacological therapy for constipation, laxatives are generally used. Laxatives can be given for a long time if there is no response to changes in diet and lifestyle. Misconceptions about bowel habits lead to excessive use of laxatives. The effect caused is hypokalemia. Magnesium oxide is a drug that is commonly given as a laxative, but because of its strong laxative effect it causes the side effect of continuous diarrhea. Apart from diarrhea, laxatives will also cause dependence and the accumulation of chemical drugs will affect. For this reason, the use of herbal plants is a safer alternative (Lestari & Suci Rahmawati, 2023).

Kate mas is a plant native to Central America and South America, whose distribution extends to tropical and subtropical areas, including Indonesia. Traditionally kate mas is used to treat constipation, bronchitis and asthma. A preliminary study of the phytochemistry of kate mas (*Euphorbia heterophylla*) leaves was carried out by (Hilma *et al.*, 2020) using the solvents n-hexane, ethyl acetate, ethanol and methanol showed the presence of alkaloids, flavonoids, saponins, tannins, diterpenes and esters. Test results using a UV-Vis spectrophotometer showed the presence of indole alkaloid compounds.

Based on research results (Somadayo *et al.*, 2015) It was found that kate mas leaf infusion had a laxative effect on male Wistar white rats (*Rattus norvegicus*) where the lower the concentration, the greater the effect obtained, seen from the frequency of defecation and fecal consistency. According to (Oktaviani *et al.*, 2017) The frequency of defecation in normal mice ranges from 3-6 times/hour with a solid fecal consistency. Based on this, the researchers wanted to conduct research on the effect of giving kate mas (*Euphorbia heterophylla* L.) leaf extract as a laxative to mice (*Mus musculus*).

## METHODS

### Time and place of research

This research was conducted in September 2022 at the Pharmacology Laboratory, Pancasakti University, Makassar.

### Research tools and materials

The tools used are mouse cages, beakers (Pyrex®), measuring cups, analytical scales, mortars, feces collection containers, maceration containers, stir sticks, oral probes, scissors, rotary evaporator. The materials used are Kate Mas leaves, 96% ethanol, Aquadest, Na CMC, 15 male mice (*Mus musculus*) weighing 20-30 grams, mouse feed, dulcolactol syrup, loperamide tab. Male mice were chosen because they tend to have consistent behavior and are much stronger than female mice. In addition, females experience hormonal fluctuations that can affect the results of the experiment (Sapitri *et al.*, 2024).

### Research procedure

#### a. Taking and processing simplicia

Kate mas leaves were taken in Lembottea hamlet, Papalang Village, Papalang District, Mamuju Regency, West Sulawesi Province. Take 4 kg of fresh kate mas leaves and sort them wetly. After that, washed in running water, then cut into small pieces using scissors. The cut leaves are then dried by airing them indoors. After drying, sorted dryly and then weighed (Pertiwi, 2022). The percentage yield of simplicia is calculated (% b/b) using the following formula:

$$\% \text{ Rendemen} = \frac{\text{berat simplisia kering}}{\text{berat sampel basah}} \times 100\%$$

#### b. Making kate mas leaf extract

Kate mas leaf simplicia is extracted by maceration using ethanol solvent. Weighed 400 grams into the maceration container, then added 4 liters of solvent. Soak for the first 6

hours, stirring occasionally, then let sit for 3x24 hours. The macerate is separated by filtration. Repeat the filtering process at least twice with the same type of solvent and half the volume of solvent in the first filtering. Collect all the macerate and concentrate it using a rotary evaporator. The thick extract obtained was then weighed (Munaeni, 2022).

c. Preparation of Na.CMC 1% w/v

A total of 1 g of Na CMC was weighed, then put into a mortar, then 20 ml of hot distilled water was added, crushed until homogeneous, then the volume was increased with distilled water to 100 ml and put into a container (Sapitri *et al.*, 2024).

d. Making a suspension of kate mas leaf extract

The dose of kate mas leaf extract is given in 3 different doses, namely, dose I, namely 70 mg/20g BW of mice, dose II, namely 140 mg/20g BW of mice and dose III, namely 280 mg/20g BW of mice. Three different doses are used, namely low dose, sufficient dose and higher dose to provide the desired effect without serious side effects. This helps in determining the optimal dose for clinical use. Then each dose of extract was weighed and then mixed with 1% Na CMC until homogeneous to a volume of 10 ml. Na.CMC is widely used in various dosage forms and extract suspensions because it can increase viscosity (Agustiani *et al.*, 2022).

e. Treatment of test animals

Laxative activity test was carried out using the Loperamide HCl induction method. The parameters used in this study were defecation recording including defecation frequency. People traditionally use 24 kate mas leaves, which is equivalent to 18.8 g/day for humans. Meanwhile, the dose for mice is 0.5 g/200 g BW (Somadayo *et al.*, 2015). Based on this research, a conversion was carried out for the body weight of mice to obtain a dose of 0.07 g/20 g BW of mice or 70 mg/20g BW of mice. In this study, mice were divided into 5 groups, 3 groups of mice positive control (Dulcolactol<sup>®</sup>), 3 mice in negative control group (Na CMC), 3 mice in test group I with a dose of 70 mg/20g BW, 3 mice in test group II with a dose of 140 mg/20g BW, 3 mice in test group III with a dose of 280 mg/ 20g BB. The test animals used were adult male mice weighing 20-30 grams. A total of 3 animals per treatment group. So in this study 15 mice were used. Before testing, mice were adapted for 7 days by continuing to be given food and fasted for 1 hour before testing. Then the mice were induced orally with Loperamide HCl tab @ 2 mg and left for 12 hours. After that, all groups were given treatment by administering ethanol extract of kate mas leaves according to the dose and group orally. Next, observe and record the frequency of defecation every hour for 6 hours (Sapitri *et al.*, 2024)

f. Data analysis

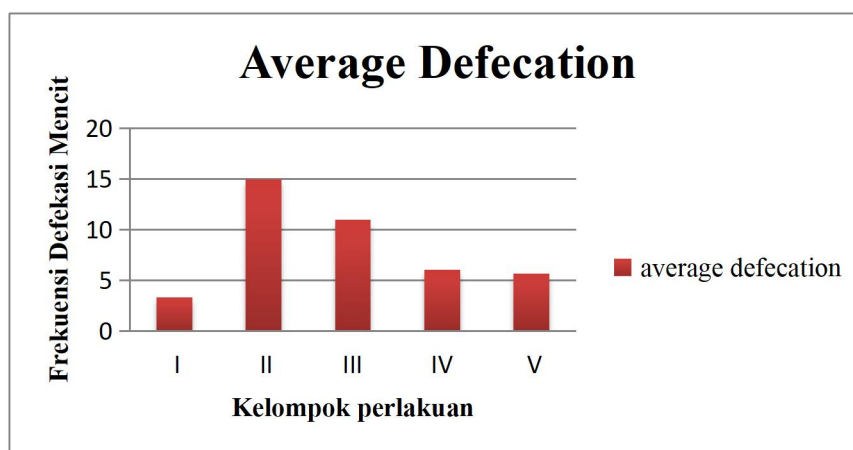
Data from observations of Kate Mas (*Euphorbia heterophylla* L.) Leaf Extract as a Laxative for Mice were statistically analyzed using the SPSS app with Non-parametric methods using the Kruskal-Wallis method with further tests using the Mann-Whitney Test method. Non-parametric tests tend to be simple in their implementation and can be applied to various types of data, so they are more flexible if the data obtained is not normally distributed (Annisak *et al.*, 2024).

## RESULT AND DISCUSSION

Based on the results of the research that has been carried out, the following results were obtained. The table shows the results of the frequency of defecation of the extract of the golden kate leaf.

Table 1. Defecation Frequency of Mice After Giving of Kate Mas Extract

Treatment	N	Frequency of Defecation after treatment in hour Ke-						Amount
		1	2	3	4	5	6	
Klp I Na CMC 1% b/v	1	1	0	1	1	1	0	4
	2	0	0	1	1	1	0	3
	3	0	1	0	1	1	0	3
$\bar{X}$								3.33
Klp II positive control	1	2	3	4	0	8	0	17
	2	1	3	3	5	1	0	13
	3	0	3	5	2	5	0	15
$\bar{X}$								15
Klp III Extract 70mg/20g BB mice	1	0	8	4	1	3	1	17
	2	0	2	0	4	2	1	9
	3	1	0	1	4	1	0	7
$\bar{X}$								11
Klp IV Extract 140mg/20g BB mice	1	1	4	0	1	1	0	7
	2	0	0	0	3	1	1	5
	3	0	0	0	2	4	0	6
$\bar{X}$								6
Klp V Extract 280mg/20g BB mice	1	0	0	0	4	1	0	5
	2	0	0	4	2	0	0	6
	3	0	0	0	3	3	0	6
$\bar{X}$								5.67



Picture 1. Histogram of average mice defecation Frequency of Mice After Giving of Katemas Extract

Information :

Group I : Negative control

Group II : Positive control

Group III : Extract kate mas leaf dose 70 mg/20 g BB

Group IV : Extract kate mas leaf dose 140 mg/20 g BB

Group V : Ekxtract kate mas leaf dose 280 mg/20 g BB

Kate mas leaf simplicia was extracted using the maceration method using 96% ethanol solvent. The maceration method was chosen because it is suitable for compounds that cannot withstand heating and has several advantages, namely that the equipment used is very simple and the work is relatively easy. Ethanol solvent was chosen because this

solvent can dissolve both polar and non-polar compounds so it is very good to use for extracting secondary metabolite compounds contained in simplicia. The 96% ethanol solvent has a small water content, namely 4%, so the resulting extract is thicker and pure.

The thick extract was suspended with Na CMC 1% w/v in three doses. Dose I is 70 mg/20 g BW of mice, dose II is 140 mg/20 g BW of mice and dose III is 280 mg/20 g BW of mice. Na CMC (Sodium Carboxymethyl Cellulose) is a cellulose derivative compound which acts as a suspending agent to increase suspension stability.

The test animals used in this study were 15 male mice which were fasted one hour before treatment. Male mice were chosen because their hormonal conditions are more stable compared to female mice which experience hormonal changes during estrus, pregnancy and breastfeeding.

The test animals were then induced with loperamide HCl tab @ 2 mg suspended with Na CMC. Loperamide works by slowing down the movement of the digestive tract so that the intestines have more time to absorb fluid, so that the frequency of defecation is reduced and the feces become denser when they come out. Loperamide is an opioid receptor agonist drug which works to reduce intestinal contractions, inhibit peristalsis and prolong transit time (Suliska *et al.*, 2019). Constipated mice can be seen when there is no defecation for approximately 1 hour and the cage bedding is clean, then they are given treatment. After being given treatment, the mice were placed in a container and covered with tissue. In one container there was only one mouse. This was done to make observation easier. The results obtained are in line with several previous studies which stated that kate mas extract can be used as an anti-inflammatory, anti-asthma and also as an anti-constipation (Hilma *et al.*, 2020).

Observations were carried out for 6 hours by recording the defecation time in each group of test animals. Mice were divided into 5 groups. Group 1 negative control, group 2 positive control, group 3 kate mas leaf extract 70 mg/20 g BW, group 4 kate mas leaf extract 140 mg/20 g BW and group 5 kate mas leaf extract 280 mg/20 g BW.

In statistical data processing, the Tests of normality show a value of ( $P < 0.05$ ), so the data in this study includes non-parametric data which is then tested using the Kruskal-Wallis Test method. In the Kruskal-Wallis Test statistical test, the frequency of defecation in mice was significant with a value of 0.016, smaller than 0.05 ( $p < 0.05$ ), thus proving that administration of ethanol extract of kate mas (*Euphorbia heterophylla*) leaves had a laxative effect on mice that were constipated. previously. The results of the follow-up Mann-Whitney Test are at group 1 (Negative control).

and group 2 (Positive control) was significant with a value of ( $P 0.046 < 0.05$ ), which means that the laxative effect in the two groups was different. Then group 1 (negative control) and group 3 (kate mas leaf extract 70 mg/20 g BW) showed significant values ( $P 0.046 < 0.05$ ), which means the laxative effect of the two groups is different. Group 1 and group 4 (kate mas leaf extract 140 mg/20 g BW) were compared and got significant results, namely ( $P 0.046 < 0.05$ ), group 1 and group 5 (kate mas leaf extract 280 mg/20 g BW) were compared and got similar results. significant, namely ( $P 0.043 < 0.05$ ). From the test results, it can be concluded that all the groups compared had different laxative effects.

The results of the follow-up Mann-Whitney Test in group 2 (positive control) and group 3 (kate mas leaf extract 70 mg/20 g BW) showed a value ( $P 0.376 > 0.05$ ), which was non-significant, which means that the two groups being compared had the same laxative effect. Group 2 and group 4 were compared to get significant results with a value of ( $P 0.05 = 0.05$ ), which means that the two groups being compared had different laxative effects. Group 2 and group 5 were compared to get significant results with values ( $P 0.046 < 0.05$ ), which means that the two groups being compared had different laxative effects.

The results of the follow-up Mann-Whitney Test in group 3 and group 4 were compared to obtain non-significant results with a value of ( $P 0.077 > 0.05$ ), which means that the two groups being compared had the same laxative effect. Group 3 and group 5 were compared to get significant results with a value ( $P 0.046 < 0.05$ ), which means that the two groups being compared had different laxative effects.

The results of the follow-up Mann-Whitney Test in group 4 and group 5 were compared to obtain non-significant results with a value of ( $P 0.637 > 0.05$ ), which means that the two groups being compared had the same laxative effect.

Based on this, it can be stated that kate mas leaf extract has an effect as a laxative with an effective dose, namely kate mas leaf ethanol extract 70 mg/20 g BW. The positive control had a higher frequency of defecation than dose I, but the positive control showed a diarrheal effect. This is because the potential laxative plant compounds begin to have an effect at lower doses. At low doses, these compounds may be sufficient to stimulate bowel movements, resulting in a laxative effect similar to that of the positive control. The digestive systems of the test animals used were sensitive even at low doses. Katemas leaves are widely used by people in Ternate, North Maluku. People use this plant as a medicine to overcome difficulty in defecating. Preliminary studies on the phytochemistry of katemas leaves extracted with n-hexane, ethyl acetate and ethanol showed the presence of active compounds flavonoids, saponins, alkaloids, tannins, diterpenes and esters (Hilma *et al.*, 2020).

## CONCLUSION

Based on the results of the research conducted, it can be concluded that the ethanol extract of kate mas (*Euphorbia heterophylla* L.) leaves has a laxative effect on mice (*Mus musculus*). The most effective concentration of kate mas leaf ethanol extract as a laxative was group 3 with a dose of 70 mg/20 g BW of mice with a defecation frequency percentage of 27% and proven by the results of statistical data analysis, the significance value of 0.376 was greater than 0.05 ( $P > 0, 05$ ).

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