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### Kawista fruit (*limonia acidissima*) extract as an alternative reduction of vomiting in pregnancy (study of laboratory in mice)

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#### ABSTRACT

##### Background

Nausea and vomiting are common symptoms in pregnancy and occur in 50-90% of pregnant women. Although mice are unable to vomit they display a gaping reaction when their serotonin levels increase. Serotonin levels in non-pregnant mice approach the lower detection threshold (0.004pmol / islet). And it increases 200 times during pregnancy. High serotonin levels can cause nausea. Vitamine B6 is believed to be a safe and effective drug to reduce nausea and vomiting in pregnancy. Kawista fruit extract has a high vitamine B6 content. Side effects on vitamine B6 drugs are severe allergic reactions (rash; hives; difficulty breathing; tightness in the chest; swelling in the mouth, face, lips, or tongue); decreased sense of touch, temperature, or vibration; loss of balance; numbness in the legs or around the mouth; numbness or tingling in the skin.

##### Objective

The aim of the study was to prove the effect of kawista fruit extract to reduce the frequency of nausea in mice.

##### Method

This study is a quantitative study that uses an experimental design model with one-group pre-test and post-test design. The number of samples used was 20 musculus mice which were divided into 4 groups, 5 controls, 5 POR, 5 kawista 0.5mg and 5 kawista 1.0mg. The examination was carried out for 6 days including gaping / gaping reflexes in mice. The sampling technique was random sampling with regard to inclusion criteria. Data analysis using Kruskal Wallis statistical test followed by Post Hoc.

##### Results

The results of this study showed a decrease in nausea and vomiting before and after intervention, the average number of gaping on day 4 in the kawista fruit treatment group was 1.0 mg, 6 times or 62% per day and value 0,000 ( $\alpha = 0, 05$ ), the average number of gaping in the kawista fruit extract treatment group dose of 0.5 mg is 7 times or 66% per day and p value 0,000 and while the POR group has an average value of nausea vomiting 8 times per day or 84% and p value 0.008.

##### Conclusions and suggestions

It can be concluded that there is an effect of consumption of kawista fruit extract to reduce nausea in mice. Based on the results of these studies it is suggested to be able to apply the use of kawista fruit especially in maternal health services.

**Keywords:** Kawista Fruit, Vomiting Nausea, Pregnancy, Gaping Reflex

## INTRODUCTION

Nausea is an unpleasant feeling related to pain or encourages vomiting, while vomiting is the excretion of gastric contents by mouth due to unconscious muscle spasm. [1].

Based on the results of the Ministry of Health RI research (2009) revealed that > 80% of pregnant women experience nausea and vomiting. The incidence of hyperemesis gravidarum also occurs in Asia such as in China, 0.9%, Pakistan 2.2%, and Turkey 1.9%. Hyperemesis gravidarum also occurs in Indonesia with incidence ranging from 1% to 3% of all trimester I pregnancies. [2]

Pregnancy nausea and vomiting, also called emesis gravidarum, occur in up to 70-85% of pregnant women, usually in the first trimester. Nausea and vomiting reduce the quality of life and cause frequent absence of work. In addition, a severe form of nausea and vomiting in pregnancy, or hyperemesis gravidarum (HG), can be considered a health risk. HG is described as hard vomiting associated with weight loss of more than 5% of pre-pregnancy body weight, dehydration and electrolyte imbalance, which can cause hospitalization. Estimates of the incidence of HG range from 0.3% -2% of pregnancy. [3]

The cause of nausea and vomiting in pregnancy is not yet known exactly, but nausea and vomiting are closely related to the etiology and pathogenesis of nausea and vomiting in pregnancy. According to the theory, physiological changes in pregnant women cause an increase in levels of human chorionic gonadotropin (hCG) and changes in psychological changes such as fear and anxiety so that they can activate the Chemoreceptor Trigger Zone (CTZ). [4]

Although the mice were unable to vomit, they displayed a distinctive gaping reaction. In fact, Travers and Norgen (1986) state that muscle movements involved in gaping responses mimic species that are capable of vomiting in displaying emetic reactions. The gaping reaction is reflected to reflect nausea and can serve as a tool used to

evaluate newly developed pharmaceuticals for nauseous side effects. [5]

In the area of West Nusa Tenggara (NTB) in general and Bima especially knows the kawista fruit only as ingredients of salad. In Indonesia this plant is rarely examined for its contents. In Indo-China, spines and kawista bark are used in various traditional medicinal herbs to treat excessive menstruation, liver disorders, animal bites and stings, and to treat nausea. [6]

## STUDY OBJECTIVES

To prove the effect of kawista fruit extract as an alternative cure for the frequency of nausea in mice

## METHODS

This research is a quantitative research that uses an experimental design model with one-group pre-test and post- test design. The number of samples used was 20 musculus mice which were divided into 4 groups: 5 controls, 5 PORs, 5 kawista 0.5mg and 5 kawista 1.0mg. The examination was carried out for 6 days including gaping / gaping reflexes in mice. The sampling technique was random sampling with regard to inclusion criteria. Data analysis using Kruskal Wallis statistical test followed by Post Hoc.

## DATA ANALYSIS

The analysis is done by univariate by calculating the mean, maximum, minimum and examination results after the first day of pvalue = 0.902 (> 0.05), until the fourth day the value of pvalue = 0.001 (<0.05). This inferential analysis was used to determine the significant differences between treatment groups. In the trial groups measurements were made > 3 times and ratio scale data with non parametric data types so that the analysis method used was Kruskal Wallis (p <0.05). Continued post hoc tests to find out the differences between groups in more detail.

## RESULTS

### Univariate Analysis

**Table 4.5 Differences in the frequency of nausea after intervention.**

interventin	Mean±SD				pvalue
	Control	POR	Kawista 0,5 g	Kawista 1,0g	
before intervention	9,6±0,5	9,6±0,5	9,6±0,5	9,8±0,4	0,890
After 1 day	9,6±0,5	9,6±0,5	9,6±0,5	9,4±0,5	0,902
After 2 day	9,6±0,5	9,4±0,5	9,2±0,4	9,2±0,4	0,513
After 3 day	9,2±0,4	8,6±0,5	8,6±0,5	8,6±0,5	0,132
After 4 day	9,2±0,4	8,4±0,5	6,6±0,5	6,2±02	0,001
After 5 day	8,6±0,5	7,6±0,5	4,6±0,5	3,8±04	0,001
After 6 day	7,6±0,5	6,4±0,8	3,4±0,5	2,2±04	0,001

\* *kruskal Wallis Test results*

In table 4.5 above it can be concluded that the frequency of nausea vomiting of mice before intervention p value = 0.890 (> 0.05), after day 1 pvalue = 0.902 (> 0.05), after the second day pvalue = 0.513 (> 0.05) and after the third day pvalue = 0.132 (> 0.05) means that there is no significant difference in the frequency of nausea and vomiting before intervention, after days 1.2

and 3. While the frequency of nausea in mice after the fourth day the value of pvalue = 0.001 (<0.05), after the fifth day pvalue = 0.001 (<0.05) and after the sixth day pvalue = 0.001 (<0.05) means that there is a significant difference in the frequency of nausea and vomiting before the intervention, after day 4.5,6.

**Table 4.6 Difference in frequency of vomiting nausea after being given an intervention in kawista fruit extract**

Dependent Variable	(I) group	(J) group	Mean Difference (I-J)	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Post.1	control	i.POR	,000	1,000	-,73	,73
		i.Kw.15	,000	1,000	-,73	,73
		i.kw.30	,200	,572	-,53	,93
		control	,000	1,000	-,73	,73
	i.POR	i.Kw.15	,000	1,000	-,73	,73
		i.kw.30	,200	,572	-,53	,93
		control	,000	1,000	-,73	,73
		i.Kw.0,5	,000	1,000	-,73	,73
	i.kw.0,5	i.kw.30	,200	,572	-,53	,93
		control	-,200	,572	-,93	,53
		i.kw.1,0	-,200	,572	-,93	,53
		i.Kw.15	-,200	,572	-,93	,53
	Control	i.POR	,200	,536	-,47	,87
		i.Kw.15	,400	,224	-,27	1,07
		i.kw.30	,400	,224	-,27	1,07
		control	-,200	,536	-,87	,47
Post.2	i.POR	i.Kw.15	,200	,536	-,47	,87
		i.kw.30	,200	,536	-,47	,87
		control	-,400	,224	-1,07	,27

Post.3	i.Kw.0,5	i.POR	-,200	,536	-,87	,47
		i.kw.30	,000	1,000	-,67	,67
		control	-,400	,224	-1,07	,27
	i.kw.1,0	i.POR	-,200	,536	-,87	,47
		i.Kw.15	,000	1,000	-,67	,67
		i.POR	,200	,490	-,40	,80
	Control	i.Kw.15	,600*	,050	,00	1,20
		i.kw.30	,600*	,050	,00	1,20
		i.POR	-,200	,490	-,80	,40

Dependent Variable	(I) group	(J) group	Mean Difference (I-J)	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Post.4	i.Kw.0,5	i.Kw.15	,400	,176	-,20	1,00
		i.kw.30	,400	,176	-,20	1,00
		control	-,600*	,050	-1,20	,00
		i.POR	-,400	,176	-1,00	,20
		i.kw.30	,000	1,000	-,60	,60
		control	-,600*	,050	-1,20	,00
	i.kw.1,0	i.POR	-,400	,176	-1,00	,20
		i.Kw.15	,000	1,000	-,60	,60
		i.POR	,800*	,022	,13	1,47
	Control	i.Kw.15	2,600*	,000	1,93	3,27
		i.kw.30	3,000*	,000	2,33	3,67
		control	-,800*	,022	-1,47	-,13
	i.POR	i.Kw.15	1,800*	,000	1,13	2,47
		i.kw.30	2,200*	,000	1,53	2,87
		control	-2,600*	,000	-3,27	-1,93
	i.Kw.0,5	i.POR	-1,800*	,000	-2,47	-1,13
		i.kw.30	,400	,224	-,27	1,07
		control	-3,000*	,000	-3,67	-2,33
	i.kw.1,0	i.POR	-2,200*	,000	-2,87	-1,53
		i.Kw.15	-,400	,224	-1,07	,27
		i.POR	1,000*	,008	,30	1,70
	Control	i.Kw.15	4,000*	,000	3,30	4,70
		i.kw.30	4,800*	,000	4,10	5,50
		control	-1,000*	,008	-1,70	-,30
	i.POR	i.Kw.15	3,000*	,000	2,30	3,70
		i.kw.30	3,800*	,000	3,10	4,50
		control	-4,000*	,000	-4,70	-3,30
Post.5	i.Kw.0,5	i.POR	-3,000*	,000	-3,70	-2,30
		i.kw.1,0	,800*	,028	,10	1,50
		control	-4,800*	,000	-5,50	-4,10
	i.kw.1,0	i.POR	-3,800*	,000	-4,50	-3,10
		i.Kw.0,5	-,800*	,028	-1,50	-,10
		i.POR	1,200*	,008	,35	2,05
	Control	i.Kw.0,5	4,200*	,000	3,35	5,05
		i.kw.1,0	5,400*	,000	4,55	6,25

Post.6	i.POR	control	-1,200*	,008	-2,05	-,35
		i.Kw.0,5	3,000*	,000	2,15	3,85
		i.kw.1,0	4,200*	,000	3,35	5,05
	i.Kw.0,5	control	-4,200*	,000	-5,05	-3,35
		i.POR	-3,000*	,000	-3,85	-2,15
		i.kw.1,0	1,200*	,008	,35	2,05
	i.kw.1,0	control	-5,400*	,000	-6,25	-4,55
		i.POR	-4,200*	,000	-5,05	-3,35
		i.Kw.0,5	-1,200*	,008	-2,05	-,35

\* *post hoc Test results*

Based on table 4.6 it can be concluded that the difference in frequency of nausea and vomiting is significant starting on the third day, four, five and six. From the third day to fourth and sixth in the first rank, the group that was given extra kawista intervention was 1.0 gr / bb with the mean difference of nausea vomiting 5.4 x / day (p value 0.000), the second rank was in the group given extra intervention kawista 0.5 gg / BB mean difference nausea vomiting 4.2 x / day (p value 0.000) and ranked third in the group given the POR intervention the mean difference nausea vomiting = 1.2 x / day (pvalue 0.008)

## DISCUSSION

Kawista fruit enriched with vitamine B6 can neutralize stomach acid and improve digestion. The B6 content in kawista fruits reduces nausea vomiting by converting protein from food to amino acids that are absorbed and needed by the body. In addition, B6 also converts carbohydrates into

energy. This role allows peridoxin to treat nausea and vomiting if gastric transit extends during pregnancy

## CONCLUSION

Kawista fruit extract has the potential to help reduce the frequency of nausea in mice compared with the POR control group (vitamine B6) as evidenced by the kruskal wallis and post hoc test. The value of p value 0.001 is less than 0.05 indicating that there are two different measurements in the group extracted kawista fruit.

## RECOMMENDATION

Future studies need to conduct pre-clinical tests to find out more about ensuring the effectiveness, safety and description of side effects that often occur in humans due to the administration of kawista fruit extract

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