

The potential effect of pandan wangi leaf “*pandanus amaryllifolius roxb.*” extract from Indonesia as time sleep inductor

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Sleep plays a role in restoring the body's biochemical and physiological processes which decrease when awake. People is not familiar yet with sleep disturbances, so they rarely seek help. Sleep disturbances can cause family problems and are at risk of fatal traffic accidents. Fragrant Pandan leaves (*Pandanus amaryllifolius Roxb.*) contains alkaloids, saponins and flavonoids which can provide a hypnotic sedative effect. The purpose of this study was to determine the effect of fragrant Pandan leaf extract (*Pandanus amaryllifolius Roxb.*) administration in shortening the sleep induction time of male Swiss Webster strain mice. A post-test only design experimental laboratory study was conducted with control group design. The test animals used were 25 Swiss Webster male mice divided into five groups randomly : G1 group was given distilled water, G2 was given diazepam dose 1 mg / KgBB, the G3, G4 and G5 groups were given fragrant Pandan leaf extract with a dose of 4 mg/25g BB, 6 mg/25g BB and 8mg/25g BB, respectively. One Way ANOVA statistical test showed significant differences in mice sleep onset ($p=0.000$) between groups. The results of the Post Hoc test using LSD analysis showed that there were significant differences between positive controls with groups G3, G4 and G5. Fragrant Pandan leaf extract dose of 8 mg/g BB can shorten the time of mice sleep induction male Swiss Webster strain mice. While the dose of 4 mg/g BB cannot shorten the time of induction of sleeping mice.

Keywords: *Fragrant Pandan leaf extract; Hypnotic-sedative; Sleep disturbances.*

INTRODUCTION

Insomnia is a disorder in the form of meet sleep needs inability, both quality and quantity. Data from the Diagnostic and Statistical Manual of Mental Disorder-IV, around 20-49% of the adult population in the United States have experienced symptoms of insomnia and it is estimated that 10-20% of them experience chronic insomnia. The collected data also concluded that women had a 1.5 times higher risk of experiencing insomnia compared to men [1] (Mai and Buysse, 2008). In Indonesia, the prevalence of insomnia is quite high, which is about 20-50% of elderly people experience insomnia and 17% experience serious sleep disorders [2] (Amir, 2016). Sleep is everyone's need. Sleep gives the brain time to recover biochemical or physiological processes that progressively decrease when awake [3] (Sherwood, 2014). Some people need to sleep less than 6 hours (short-sleeper) and less than 9 hours (long-sleeper) at night to function adequately [4] . (Sadock & Sadock, 2010).

One of the drugs used to treat insomnia is sedative-hypnotic. Sedatives are drugs that can reduce anxiety and have a calming effect with little or no effect on motor or mental function. Hypnotics can

cause drowsiness, prolong and maintain sleep. The ideal hypnotic should cause sleep, such as physiological sleep, and not change sleep patterns pharmacologically, cause no effects on tomorrow, rebound anxiety, or sustained sedation. The hypnotic effect can be easily obtained by increasing the dosage of sedative drugs. At even higher doses, hypnotic-sedative drugs can suppress the respiratory system and vasomotor center in the medulla, leading to coma and death. Some of these classes of drugs are barbiturates and benzodiazepines. The continuous and irrational use of currently available hypnotic-sedative drugs can cause physical dependence and withdrawal symptoms [5] (Katzung, 2013).

Indonesia has abundant medicinal plants, but only 2.5% is used as traditional medicine [6]. (Khotimah, 2016). World Health Organization (WHO) recommends the use of traditional medicines in the maintenance of public health, prevention and treatment of diseases. WHO also supports efforts in improving the safety and efficacy of traditional medicines [7]. (WHO, 2016). The use of traditional medicine in general is considered safer than the use of modern medicine. This is because traditional medicines have relatively fewer side effects than modern drugs [8] (Bustanussalam, 2016). Indonesia as a tropical country has a wealth of medicinal plants. One of the plants used for traditional medicine is fragrant pandanus (*Pandanus amaryllifolius* Roxb). Fragrant pandanus is found throughout most of Indonesia, especially in the tropics and is mostly planted in the yard or in the garden. In previous studies, it was known that fragrant pandan extract at certain doses has sedative-hypnotic effects. However, evidence of the effects of fragrant pandan extract can shorten sleep induction time is not clearly known.

MET HODS

Study design: This research is a laboratory experimental study with a post test only with control group design.

Ethical approval: This research Approved by Health Research Ethics Committee Faculty of Medicine University Muhammadiyah Surakarta in Ethical Clearance Letter No. 1195/A.1/KEOK-FKUMS/2018

Sample size: The animals used were 25 Swiss Webster male mice

Grouping: Divided into five groups randomly in each group n=5

Drug administration: The G1 group was given aquadest, the G2 group was given a dose of diazepam 1 mg / KgBB, the G3, G4, and G5 group was given 4 mg / gBB, 6 mg / gBB, and 8 mg / gBB fragrant Pandan leaf extract, respectively.

Parameters studied: The onset of sleep was measured as a hypnotic-sedative effect.

Statistical analysis: The results of the study were analyzed using One Way ANOVA test with normal data distribution and homogeneous variants requirements, then continued with a Post Hoc test.

RESULTS

The hypnotic-sedative effect of fragrant Pandan leaf extract (*Pandanus amaryllifolius* Roxb.) on Swiss Webster strain mice shown in Table 1.

Table 1. Sleep onset of mice in each group (minutes)

No	G1(-)Aquadest	G2(+)Diazepam	G34mg/gBB	G46mg/gBB	G58mg/gBB
1	80	23	65	45	42

2	106	18	79	40	39
3	100	23	68	48	40
4	115	30	60	47	40
5	109	29	58	51	38
	102	24,6	66	46,2	39,8

Table 1.

These data shown that group G5 has faster sleep onset than group G3, G4 and G1 (-), sleep onset of G4 group was faster than G3 and G1 (-), and sleep onset of group G3 was faster than G1 (-) as shown in the Table 1. These results indicate that fragrant Pandan leaf extract (*Pandanus amaryllifolius* Roxb) at a dose of 8 mg / g BB has a faster effectiveness in inducing mice sleep time compared to a dose of 4 mg / g BB and 6 mg / g BB. The results of the normality test with Saphiro Wilk and the homogeneity test with Levene Test showed normal and homogeneous data distribution ($p > 0.005$).

Data analysis using One Way Annova obtained p value = 0,000 ($p < 0.05$) which means that there are significant differences between groups so that the hypothesis can be accepted. Post Hoc test results using the LSD (*Least Significant Difference*) test to find out the significant differences between groups can be seen in Table 2.

Table 2. Least Significant Difference (LSD) on mice sleep onset

Group	p value	
G1(-) - G2(+)	0.000	different significantly
G1(-) - G3	0.000	different significantly
G1(-) - G4	0.000	different significantly
G1(-) - G5	0.000	different significantly
G2(+) - G3	0.000	different significantly
G2(+) - G4	0.000	different significantly
G2(+) - G5	0.005	different significantly
G3 - G4	0.001	different significantly
G3 - G5	0.000	different significantly
G4 - G5	0,201	not different

Table 2.

($p < 0.05$ = different significantly; $p > 0.05$ = not different)

The results of the statistical test ($p < 0.05$) was proved that fragrant Pandan leaf extract (*Pandanus amaryllifolius* Roxb.) has an effect on the time of induction of mice sleep.

DISCUSSION

The content of fragrant Pandan leaf extract is thought to have important compounds, namely flavanoids, alkaloids and saponins. Flavanoids are a class of phenyl propanoid compounds with a carbon frame C6-C3-C6. It is non-polar but has a sugar group which causes flavanoids to dissolve in polar solvents [9]. (Fidiyani *et al.*, 2015). Flavanoids have a sedative effect mediated by GABA ionotropic specifically through benzodiazepine binding sites [10] (Hanrahan *et al.*, 2011). The amentoflavone component of the flavanoids can modulate the GABA-A receptor and show high affinity for the benzodiazepine binding site [11] (Wasowski & Marder, 2012). Since the benzodiazepine binding site is bound, the GABA-A receptor will be mediated and active so that the

chloride canal is opened which causes hyperpolarization and the effect is drowsiness to sleep [10]

Alkaloids can induce sedative effects by binding directly to GABA-A receptors. (S) -reticuline acts as a positive allosteric modulator in $\alpha 3$, $\alpha 5$, and $\alpha 6$ isoforms of GABA-A receptors. When GABA-A ionotropic receptors are bound there will be cell hyperpolarization resulting in a reduction in action potential where it will provide a hypnotic-sedative effect [12,13] (Feducuro, 2015; Ikawati, 2006). Saponins are polar compounds that bind to GABA-A receptors. The bond causes the chloride canal to open and hyperpolarization occurs and decreases excitation, causing drowsiness even to sleep [9, 14,15], (Purnomo, 2004; Shalabi & Sana, 2012; Fidiyani *et.al*, 2015).

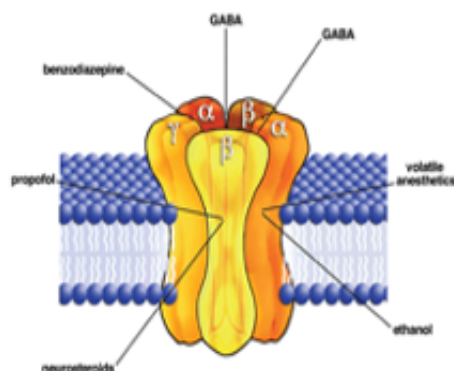


Figure 1. GABA receptor [16] (Lovinger, 2008)

Gamma-aminobutyric acid (GABA) is an amino acid that functions as the main neurotransmitter inhibitor in the central nervous system (CNS). Nearly 40% of synapses in the central nervous system are GABA neurotransmitters, and GABA-A receptors can be found almost throughout the surface of the brain [17] (Mohler, 2001). GABA has several types of receptors, namely, GABA-A, GABA-B and GABA A-rho or previously known as GABA-C [18] . (Olsen & Sieghart, 2008). When the GABA-A receptor is activated, there will be a hyperpolarizing effect of neurons and result in a reduction in action potential. GABA receptors, some of their allosterics and GABA-A receptor subtypes are the main targets of analgesic, anxiolytic and sedative drugs [19] (Ramachandran & Shekhar, 2011). Activation of the GABA receptor has caused central nervous system depression effects such as sedative, hypnotic and anticonvulsant effects [13, 20] (Bateson, 2004; Ikawati, 2006). Sedation is a resting state, and hypnotics is a continuation of sedation, namely the onset of drowsiness and causes the onset of natural sleep [21] (Grace, 2007). Judging from the daily life of sleep can be influenced by environmental health status, psychological stress, diet, lifestyle and drugs [22] (Asmadi, 2008).

CONCLUSION

Fragrant Pandan leaf extract (*Pandanus amaryllifolius* Roxb.) dose of 8mg/gBB and 6mg/g BB can shorten the sleep induction time of Swiss Webster strain mice, while a dose of 4 mg / g BB cannot shorten sleep induction time.

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