Analgesic Activity of Ethanol Extract of *Rhaphidophora pinnata* L.f Schott Leaves in Mice Induced by Acetic Acid

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Abstract: *Rhaphidophora pinnata*, Araceae Family, were suspected able to reduce pain. This study aimed to determine the effect of *Rhaphidophora pinnata* to reduce pain by acetic acid induced writhing response in mice. This effect was examined by the acetic acid induced writhing response in mice. The animals were divided into five groups (n=5) and received ethanol extract of *Rhaphidophora pinnata* leaves at doses of 50, 100 and 200 mg/kg BW, Sodium CMC 0.5% as negative control and acetosal 200 mg/kg BW as positive control. These preparations were given orally 30 minutes before the given acetic acid 3% (w/v) as the pain inductor. Analgesic activity was measured by counting the percentage of writhing movements. The study showed that all of dose ethanol extract of *Rhapidophora pinnata* gave significant pain reduction in mice induced by acetic acid ($p<0.05$) compared to control group. The effective dose was shown by ethanol extract of *Rhaphidophora pinnata* 50 mg/kg BW. Ethanol extract of *Rhaphidophora pinnata* leaves can reduce pain in mice induced by acetic acid.

1 INTRODUCTION

Rhaphidophora pinnata, Araceae Family, has been traditionally used to relieve pain,cough, anti anemia and antirheumatic. Some study have been conducted on this plant to prove its pharmacology activities such as bacterial infection, cytotoxic and antimutagenic. Chloroform fraction of this plant can inhibit proliferation on MCF-7 cell line (Masfria, 2015; Masfria, et al, 2017; Sumaiyah, et al, 2018). This effect arises because *Rhaphidophora pinnata* leaves contained some active compound such as flavonoids, alkaloids, glicoside tannins and saponins (Masfria, et al, 2017). Flavonoids may be responsible for inhibition of cyclooxygenase (COX) enzyme in some plant. Sixty-four papers were found concerning the potential analgesic activity of 46 flavonoids (Xiao, et al, 2016).

COX is enzyme that is responsible for the formation of prostaglandin from arachidonic acid and cause pain when the body tissue damage. If pain disturbs activity of the body, an analgesic drug is used for the relief of pain without losing consciousness (Hasimun, et al, 2014). Conventional analgesic drug can cause acute or chronic renal damage when it is used frequently. So, there is a need for effective analgesic without causing much of adverse effects. This study aimed to determine the effect of *Rhaphidophora pinnata* to reduce pain by acetic acid induced writhing response in mice.

2 METHODS

2.1 Materials

Rhapidophora pinnata leaves were collected from Medan, Sumatera Utara, Indonesia and authenticated by Biological Department of Faculty of Math and Science, University Sumatera Utara, Medan. The other chemical was used in this study: Acetosal (Bayer), Acetic Acid 3% (Merck), Normal saline (Widatra Bakti), and ethanol 96% pro analysis.

2.2 Preparation of Plant Extract

The dried powder of *Rhaphidophora pinnata* leaves were extracted by ethanol 96% using percolation

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method. The percolat was concentrated in a rotary evaporator until obtained the thick extract.

2.3 Analgesic Activity of *Rhaphidophora pinnata*

Animals were allowed to acclimate for 14 days in the cage separately before getting treatment. All of animals has been given permission by the Institutional Animal Ethical Committee of Biological Department Of Faculty of Math and Science, University of Sumatera Utara, Medan. Fifty five of mice were randomly divided into 5 groups of five animals each. Every group was treated as follows: (1) Sodium CMC 0.5% as negative control; (2) Acetosal 200 mg/kg BW as positive control; ethanol extract of *Rhaphidophora pinnata* (EERP) at dose 50, 100, and 200 mg/kg BW, respectively for group of 3-5. This preparation were given orally 30 minutes before the given 0.5 mL/20 g BW acetic acid 3% (w/v) as the pain inductor and then all of the animals were observed for writhing behavior which indicated by muscular contractions and counted every 10 minutes for 60 minutes (Hasimun, et al, 2014; Manivannan and Aeganathan, 2016).

The percent protection of analgesic was calculated using the formula:

$$\% \text{ protection} = 100 - \{ (Wt / Wn) \times 100\% \} \quad (1)$$

Where,
Wn = Number of writhes in negative control group,
Wt = Number of writhes in test group

The percent effectivity of analgesic was calculated using the formula:

$$\% \text{ Effectivity} = \{ (Wt / Wp) \times 100\% \} \quad (2)$$

Where,
Wp = Number of writhes in positive control group,
Wt = Number of writhes in test group

2.4 Statistical Analysis

All of experimental data were expressed in multiple comparisons of Mean ± SEM. Data were analyzed statistically by ANOVA and considered significant at $P < 0.05$.

3 RESULTS

The acetic acid-induced writhing method was a sensitive test to evaluate the effect of analgesics drugs on visceral pain by releasing endogenous mediators indirectly that stimulate nociceptive neurons such as prostaglandins into peritoneum (Xiao, et al, 2016; Hasimun, et al, 2014). In this study, the analgesic effect of EERP in the acetic acid-induced writhing model was shown in Fig 1.

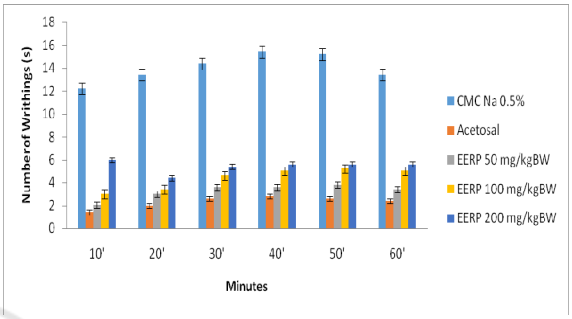

Figure 1. Number of writhings of acetic acid induced writhing for 60 minutes

The number of writhing responses were significantly reduced in mice treated at dose of 50, 100 and 200 mg/kg BW compared to negative control. But there were not increasing analgesic activity by increasing doses. It means that effective dose of EERP as analgesic was 50 mg/kg BW.

The percent protection of writhing was a parameter that describes the protection of extract against pain compared to the control. The percent protection of pain of the treated group was calculated from the mean writhing count of the treated group and control group (Hasimun, et al, 2014; Marivannan and Aeganathan, 2016). The result showed that EERP can protect the pain by 74.58, 60.41 and 55.647% compared to control whereas acetosal showed 81.55% (Fig. 2).

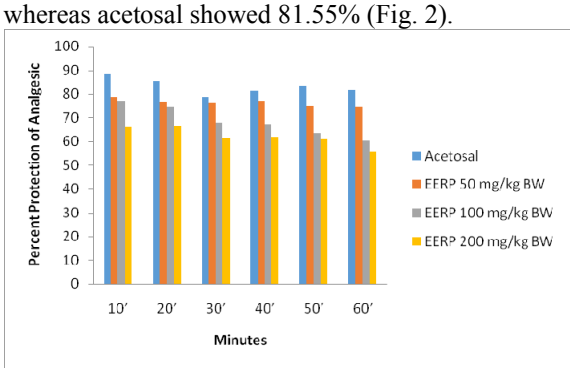

Figure 2. The percent protection of analgesic of EERP

The percent of effectivity of analgesic of EERP were shown in Fig 3. The data showed that percent effectivity of EERP 50, 100 and 200 mg/kg bw were 92.80, 73.39, and 68.30 % respectely.

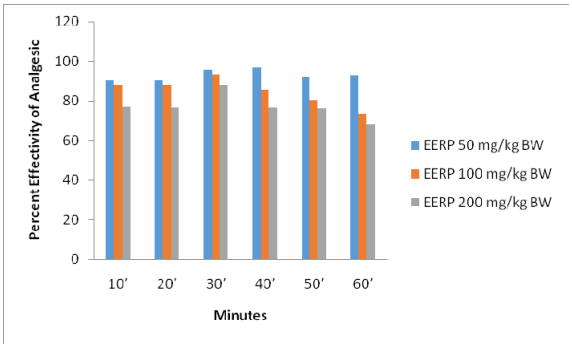

Figure 3. The percent effectivity of analgesic of EERP

One of the active compound that contained by *Rhaphidiphora pinnata* is flavonoid. Flavonoid inhibits the release of endogenous substances (arachidonic acid metabolites) in inflamatory processes. Previous study showed that quercetin, myricitrin, hesperidin, and dihydroxy flavones have analgetic activity through some mechanism like inhibition of cytokine and prostglandin production or inducing nitrooxide production (Waldiceu, et.al, 2012). The result of this experiment alleged that The mechanism of *Rhaphidophora pinnata* as analgesic was mediated by peripheral process (Hasimun, et al, 2014; Manivannan and Aeganathan, 2016; Hijazi, et al, 2017; Couto, et al, 2011).

4 CONCLUSION

The study concluded that ethanol extract of *Rhaphidophora pinnata* leaves can reduce pain in mice induced by acetic acid.

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