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Analgesic activity of ethanol extract of Lantana camara

Ifora Ifora[1]*, Saras Alvionita Putri[1], Widya Kardela[1]
[1]*Department of Pharmacology and Clinical Pharmacy, School of Pharmaceutical Science Padang (STIFARM Padang), West Sumatera, Indonesia, 25147.*

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ABSTRACT:
Pain is an uncomfortable sensory and emotional experience that is associated with or described in terms of actual or potential tissue damage. The most common reason for a patient's visit to the doctor is pain.However, conventional painkillers are ineffective in treating all types of pain, additional efforts have been made to develop analgesic drugs from natural materials. In this study, the ethanolic extract of Lantana camara (EELc) was examined for its antinociceptive activity at doses of 140, 280, and 560 mg/kg body weight. Acetic acid-induced writhing was used to evaluate the antinociceptive activity of EELc. The results showed that the EELc(140, 280, and 560 mg/kg BW) had significant antinociceptive activity. The percentage of inhibition was 25%, 33%, and 39%, respectively. These findings imply that Lantana camara leaf extracts have promising antinociceptive properties.
KEYWORDS: Antinociceptive, Lantana camara, Ciplukan, Analgesic.

I. INTRODUCTION

Pain is an unpleasant sensation that is usually brought on by intense or harmful stimuli. It is also defined as a distressing sensory or emotional experience linked to actual or potential tissue damage.[1]. Pain is defined as a multidimensional experience that includes many components and has motivational, emotional, sensory-discriminative, affective, and cognitive aspects[2], [3]. Sometimes for the diagnosis of several diseases, pain is the only symptom[4], [5]. Throughout history, man has used many forms of therapy for pain relief, among which, medicinal plants are highlighted due to their widespread and popular use[6]–[9]. An example is, Papaver somniferum from which morphine was isolated[10]. Though morphine is considered the prototype of opioid analgesics, it presents considerable side effects such as respiratory depression, sleepiness, decreased gastrointestinal motility, nausea, and endocrine and autonomic nervous systems disorders [11], [12]. The exploration of natural compounds with comparable analgesic activity but fewer side effects is important..

Lantana camara L., commonly known as wild or red sage, is the most widespread species of this genus, growing luxuriantly at elevations up to 2000 m in tropical, sub-tropical, and temperate regions[13]. The plant has been used in many parts of the world to treat a wide variety of disorders[14]. Lantana camara found use in folk remedies for cancers and tumors. A tea prepared from the leaves and flowers was taken against fever, influenza, and stomachache. In Asian countries, leaves were used to treat cuts, rheumatisms, and ulcers, and as a vermifuge[13]. In addition, other ingredients were found, such as triterpenes, β-sitoterolol, and Falvonoids[15], [16].

Lantana camara leaf extract is believed to have, anti-aging, antimicrobial, anti-inflammatory, anti-cancer, and nematicidal[17]–[20]. In the current study, we have now evaluated the potential analgesic activity of the ethanolic extract of Lantana camara leaf on acetic acid-induced writhing models.

II. MATERIALS AND METHOD

Materials

The following drugs and chemicals were used in the current study: ethanol 70% (PT. Novalindo), Aspirin (acetylsalicylic acid) (PT. Darya-Varia Laboratoria Tbk), Acetic acid (Merck, Germany) and other reagents were purchased from Bratachem (Indonesia).

The Lantana camara leaveswere collected from Limau Manih, Padang, West Sumatera. The Lantana camara were identified by Dr. Nurainas, a botanist at the Herbarium of Andalas University, West Sumatera, Indonesia.

Preparation of The Ethanol Extract of Lantana camara(EELc)

The Lantana camara leaves were sun-dried. The dried Lantana camara was powdered using a conventional grinder. The powdered

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materials were then soaked in ethanol (70%) for 24 hours by stirring at room temperature. The materials were filtered after 24 hours. The procedure was repeated three times. The filtrates were mixed and concentrated under a vacuum using a rotary until free of solvent. The extract was kept cold for further pharmacological testing.

Phytochemical screening

EELc was qualitatively tested for the detection of saponins, flavonoids, Phenolic, tannins, alkaloids, phenolic, terpenoids, and steroids following standard procedures [21].

Experimental Animal

25 adult male mice with body weights of 20–25 g and aged 2-3 months were obtained from West Sumatera animal houses and were used for this study. Animals were housed and cared for in standard conditions with 12 h light/dark circle and were fed with a standard pellet diet and water ad libitum. All the animals were acclimatized for a minimum period of 1 week prior to the experiment. After 1 week, animals were randomly selected for different experimental groups (5 animal/ group) and used for the in vivo determination of antinociceptive activity. The rats were deprived of food, but not water, for 18–20 hours before an experiment. The protocol of this experiment was approved by The Committee of The Research Ethics of The Faculty of Medicines, Andalas University (permit No. 057/KEP/FK/2020).

Analgesic activity:

Acetic acid-induced writhing model was used for evaluating the potential of ethanolic extract of the plant on pain. In this method, pain was produced by the administration of 1% v/v of acetic acid (1mL/100g body weight of mice). The mice were placed in separate boxs under observation immediately after the acetic acid injection and a number of abdominal constrictions were counted over a period of 60 min. [16] The experimental protocol comprises as follows:

Group I (Control, Na.CMC 0,5%)
Group II was treated with EELc (140mg/kgBW, orally)
Group III was treated with EELc (280mg/kgBW, orally)
Group IV was treated with EELc (560mg/kgBW, orally)
Group IV was treated with Aspirin (65mg/kgBW, orally).

The groups used for observing the influence of ethanolic extract on 1% v/v of acetic acid-induced writhing in mice. Stretching movements consisting of arching of the back, elongation of body and extension of hind limbs were counted.

The percentage protection was calculated by following the formula:

$$\% \text{ Analgesic Activity} = \frac{\text{Mean writhing count (control} - \text{Treated)}}{\text{Mean writhing count control}} \text{ x } 100$$

Statistical Analysis

The statistical software SPSS version 25 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Data were analyzed using one-way ANOVA followed by Duncan's multiple range test. In all tests, the criterion for statistical significance was $p < 0.05$.

III. RESULTS

Phytochemical screening

In the present study, preliminary phytochemical screening tests of the crude extract showed the presence of alkaloids, flavonoids, saponins, terpenoids, phenolic and tannins. (Table 1).

Table 1. Phytochemistry screening test result of Lantana camara

Groups	Result
Alkaloid	+
Falvonoid	+
Saponin	+
Steroid	-
Terponoid	+
Phenolic	+
Tannin	+

Analgesic activity

Lantana camaraleaves presented significant antinociception to the control group in test models of nociception induced by chemical agents. In the acetic acid-induced writhing test, performed in the present study, EELc in the doses

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of 160, 280 and 560 mg/kg, p.o., significantly reduced the number of writhes (31,6 ± 3,2;28,6 ± 2,3; and 25,8 ± 2,2writhes/60 min), respectively, in relation to the control group (42 ±7,43writhes/20 min) (Fig. 1). The Aspirin (65 mg/kg, p.o.), a nonsteroidal anti-inflammatory drug, also promoted a significant reduction in the number of writhes (23,2 ± 1,1 writhes/60 min). The percentage inhibition of pain was calculated as 45% (Aspirin), 25% (EELc 140 mg/kg), 33% (EELc 280 mg/kg), and 39% (EELc 560 mg/kg) (Table 2).

Tabel 2. Analgesic Activity by Acetic Acid Induced Writhing in Mice of Lantana camara

Gruops	Treatment	Dose (mg/kg B.W)	Writhings	(%)inhibition[a]
I	Control (Na. CMC 0,5% + Acetic Acid 1%)	-	42 ±7,43	-
II	EELc	140	31,6 ± 3,2	25*
III	EELc	280	28,6 ± 2,3	33*
IV	EELc	560	25,8 ± 2,2	39*
V	Aspirin[b]	65	23,2 ± 1,1	45*

[a]Data are expressed as the mean of Three observations (n = 5), [b]Used as comparative group
*** Significant difference compared to the positive control (P < 0.05)**

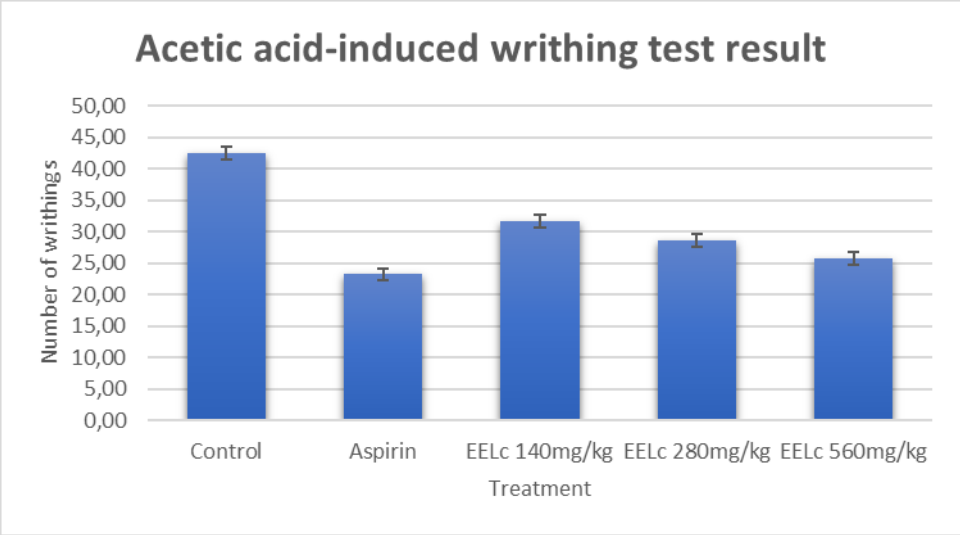

Figure 1. The antinociceptive effect of ethanol extracts Lantana camaraon the acetic acid-induced writhing test.

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IV. DISCUSSION

The current study shows that administering EELc orally has a potent and dose-dependent antinociceptive effect in chemical-induced nociception models. In the acetic acid-induced writhing test, performed in the present study, EELc in the doses of 160, 280 and 560 mg/kg, p.o., significantly reduced the number of writhes.

The writhing action in mice caused by an intraperitoneal injection of acetic acid in chemical nociception is used to assess central and peripheral analgesic activity..

Acetic acid administered intraperitoneally raises the levels of cyclooxygenase (COX), lipoxygenase (LOX), prostaglandins (PGs), histamine, serotonin, bradykinin, substance P, IL-1 beta, IL-8, and TNF alpha in peripheral tissue fluid[22].Increased level of these mediators causes the excitation of primary afferent nociceptors entering dorsal horn of the central nervous system[23].

In accordance with the percentage of inhibition of the number of the writhes obtained through Lantana camara use, it was observed that the intensity of its analgesic effect was significantly similar to the Aspirin. The Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) can inhibit cyclooxygenase in peripheral tissues reducing the synthesis and/or the release of inflammatory mediators intervening thus, with the mechanisms of transduction of primary afferent nociceptors[24]. The analgesic mechanism of action of the Lantana camara can, probably, involve inhibition of the synthesis and/or release of inflammatory mediators who promote pain in the nervous terminations, similarly to the Aspirin and the other NSAIDs suggesting a peripheral analgesic action. However, the test of abdominal constrictions is non-specific, since NSAIDs and opioid analgesics may inhibit the nociceptive response in the acetic acid model[25], [26].

According to our phytochemical screening results, EELc contains terpenoidOther studies suggested that plant materials that contain triterpenoidpossess analgesic and anti-inflammatory effects on experimental animals and these pharmacological effects are resulted from these contents[8], [27]–[31]. Additionally, different terpenoids have been found to be antinociceptive and anti-inflammatory agents due to their ability to inhibit arachidonic acid metabolism[28], [32]–[35]. Therefore, it is possible that the presence of terpennoids in the EELc may be responsible for the antinociceptive effect.

V. CONCLUSION

Lantana camara leaf ethanol extract had a significant and dose-dependent analgesic effect. More research is needed to confirm this preliminary finding, which may lend support to some of the plant's uses in Indonesian herbal medicine practice.

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