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Antinociceptive Effect of Ethanol Extract of *Physalis Angulata*

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ABSTRACT

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is the most common reason a patient sees a physician. However, conventional painkillers are not completely effective in controlling all pain syndromes; thus, additional efforts have been made to develop analgesic drugs from natural materials. In this study, the ethanolic extract of *Physalis angulata* (EEA) 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 EEPa. The results showed that the EEPa (140, 280, and 560 mg/kg BW) had significant antinociceptive activity. The percentage of inhibition was 29,41%, 37,96%, 44,38%, respectively. These findings suggest that *Physalis angulata* leaves extracts possess promising antinociceptive effects.

KEYWORDS: Antinociceptive, *Physalis angulata*, Ciplukan, Analgesic.

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INTRODUCTION

Pain is an unpleasant sensation usually caused by intense or damaging stimuli. It is also defined as an unpleasant sensory or emotional experience associated with actual or potential tissue damage [1]. Pain is described as a multidimensional experience with many components involved and having 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 discovery of natural compounds that have similar analgesic activity, yet with fewer side effects is pertinent.

Physalis angulata L. (known in Indonesia as 'Ciplukan') is a member of the genus Physalis (Solanaceae) comprising approximately 120 species widely distributed in tropical and subtropical regions [13]. As a traditional folk medicine, *P. angulata* has been used to cure inflammatory-related diseases, such as dermatitis, asthma, hepatitis, and malaria in other countries such as India and indonesia[14].The active substance successfully isolated from *Physalis angulata* leaf extract is physalin, which is a derivative of flavonoid glycosides[15,16]. In addition, other ingredients were found, such as quercetin, α-Tocopherol, and withanolides[13,17,18]. *Physalis angulata* leaf extract is believed to have, antimicrobial, anti-inflammatory, anti-cancer, antioxidant, and immunosuppressive potential[13,19–21]. In the current study, we have now evaluated the potential analgesic activity of the ethanolic extract of *Physalis angulata* leaf on acetic acid-induced writhing models.

MATERIALS AND METHOD

Materials

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

The *Physalis angulata* leaves were collected from Kerinci, Jambi, Indonesia. The *Physalis angulata* were identified by

Dr. Nurainas, a botanist at the Herbarium of Andalas University, West Sumatera, Indonesia.

Preparation of The Ethanol Extract of *Physalis angulata* (EEPa)

The *Physalis angulata* leaves were sun-dried. The dried *Physalis angulata* was powdered using a conventional grinder. The powdered 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

EEPa was qualitatively tested for the detection of saponins, flavonoids, tannins, alkaloids, phenolic, terpenoids, and steroids following standard procedures [22].

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. 063/KEP/FK/2020).

Antinociceptive 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 EEPa (140mg/kgBW, orally)
Group III was treated with EEPa (280mg/kgBW, orally)
Group IV was treated with EEPa (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:

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

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 $p < 0.05$.

RESULTS

Phytochemical Screening

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

Table 1. Phytochemistry screening test result of *Physalis angulata*

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

Antinociceptive Activity

Physalis angulata leaves 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, EEPa in the doses of 160, 280 and 560 mg/kg, p.o., significantly reduced the number of writhes (26.4 ± 3.20;23,2 ± 1,92; and 20,8 ± 2,16 writhes/60 min), respectively, in relation to the control group (37,4 ±7,43 writhes/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 (18,2 ± 1,09 writhes/60 min). The percentage inhibition of pain was calculated as 51.33% (Aspirin), 29.41% (EEPa 140 mg/kg), 37.96% (EEPa 280 mg/kg), and 44.38% (EEPa 560 mg/kg) (Table 2).

Tabel 2. Analgesic Activity by Acetic Acid Induced Writhing in Mice of *Physalis angulata*

Gruops	Treatment	Dose(mg/kg B.W)	Writhings	(%) inhibition[a]
I	Control (Na. CMC 0,5% + Acetic Acid 1%)	-	37,4 ±7,43	-
II	EEPa	140	26,4 ± 3,20	29,41*
III	EEPa	280	23,2 ± 1,92	37,96*
IV	EEPa	560	20,8 ± 2,16	44,38*
V	Aspirin[b]	65	18,2 ± 1,09	51,33*

[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)**

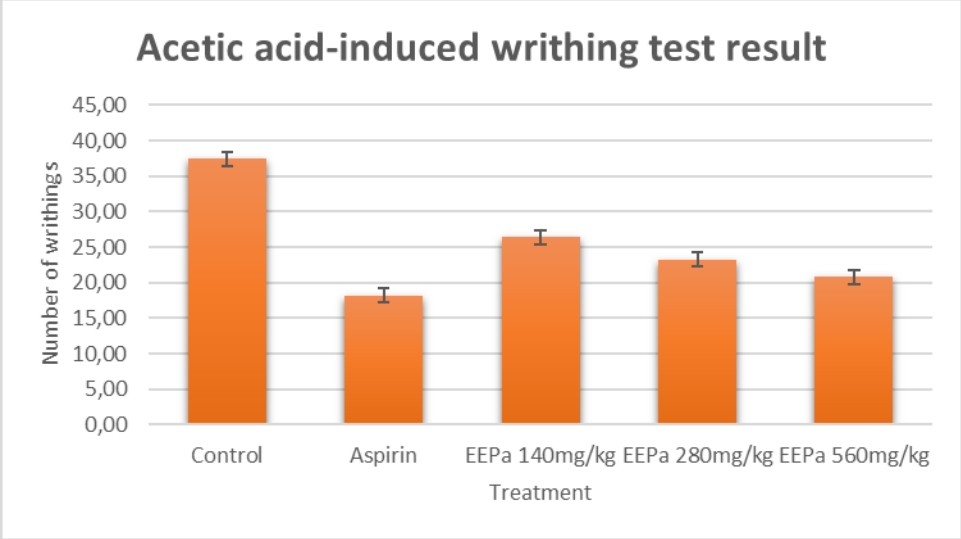

Figure 1. The antinociceptive effect of ethanol extracts Physalis angulata on the acetic acid-induced writhing test.

DISCUSSION

The present study demonstrates that oral administration of EEPa elicits a potent and dose-dependent antinociceptive effect in chemical-induced nociception models. In the acetic acid-induced writhing test, performed in the present study, EEPa in the doses of 160, 280 and 560 mg/kg, p.o., significantly reduced the number of writhes.

The writhing behavior, in mice, by the intraperitoneal injection of acetic acid in the chemical nociception, is used to evaluate, essentially, central and peripheral analgesic activity.

Intraperitoneal administration of acetic acid causes an increase in the level of cyclooxygenase (COX), lipoxygenase (LOX), prostaglandins (PGs), histamine, serotonin, bradykinin, substance P, IL-1 beta, IL-8, TNF alpha in the peripheral tissue fluid. 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 *Physalis angulata* use, it was observed that the intensity of its analgesic effect was significantly similar to the Aspirin. The Aspirin and other nonsteroidal antiinflammatory 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 *Physalis angulata* 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].

Our phytochemical screening results indicated that EEPa contains phenolic compounds such as flavonoids and tannins. Other studies suggested that plant materials that contain tannins, alkaloids, flavonoids, and phenolic acids possess analgesic and anti-inflammatory effects on experimental animals and these pharmacological effects are resulted from these contents[18,27–29]. It was suggested that flavonoids demonstrate an antinociceptive effect through opioid mechanisms[30,31]. Additionally, different flavonoids have been found to be antinociceptive and anti-inflammatory agents due to their ability to inhibit arachidonic acid metabolism[32,33]. There are few reports on the role of tannins in antinociceptive and anti-inflammatory activities[8,34]. Therefore, it is possible that the presence of

flavonoids and tannin in the EEPa may be responsible for the antinociceptive effect. A positive result with this test is indicative of antinociceptive activity in the EEPa, although it remained to be determined whether this activity is of central or peripheral origin.

CONCLUSION

The ethanol extract of *Physalis angulata* leaves showed a significant and dose-dependent analgesic effect. Further studies are required to confirm this preliminary finding which may also lend support to some uses of the plant in Indonesian herbal medical practice.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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REFERENCES

I. Loeser JD, Melzack R. Pain: An overview. Lancet. 1999;353(9164):1607–9.
II. Woolf CJ. What is this thing called pain? Fam Matters. 2010;120(11):77–9.
III. Robertson SA. “What Is Pain?” Lancet. 1887;130(3337):333–4.
IV. Foley KM. The relationship of pain and symptom management to patient requests for physician-assisted suicide. J Pain Symptom Manage. 1991;6(5):289–97.
V. Emanuel EJ. PAIN AND SYMPTOM CONTROL Patient Rights and Physician Responsibilities. PAIN Palliat CARE. 1996;10(1):41–56.
VI. Uritu CM, Mihai CT, Stanciu GD, Dodi G, Alexa-Stratulat T, Luca A, et al. Medicinal plants of the family Lamiaceae in pain therapy: A review. Pain Res Manag. 2018;2018.
VII. Mulia A, Oktavia S, Ifora I. Pharmacological Properties of Δ (9) Tetrahydrocannabinol: A Review. EAS J Pharm Pharmacol. 2021;3(1):13–20.
VIII. Auliana FR, Ifora I, Fauziah F. Phytochemical and Anti-Inflammatory of Uncaria gambir: A Review. Asian J Pharm Res Dev. 2022;10(1):79–83.
IX. Souri MS, Oktavia S, Ifora I. Potential anti-inflammatory effects of Psidium guajava L.: A review. Asian J Pharm Res Dev. 2021;9(2):47–52.
X. Trang T, Al-Hasani R, Salvemini D, Salter MW, Gutstein H, Cahill CM. Pain and poppies: The good, the bad, and the ugly of Opioid analgesics. J Neurosci. 2015;35(41):13879–88.
XI. Andersen G, Christrup L, Sjøgren P, Royal T. Relationships Among Morphine Metabolism , Pain and Side Effects During Long-Term Treatment : An Update. 2003;25(1):74–91.
XII. Martínez MA, Ballesteros S. Opium poisoning in modern times . An overview. Forensic Sci Int [Internet]. 2019;302:109848. Available from: https://doi.org/10.1016/j.forsciint.2019.06.006
XIII. Pillai JR, Wali AF, Menezes GA, Rehman MU, Wani TA, Arafah A, et al. Antioxidant Activities of Physalis angulata L .: A Comparative Study of Leaves and Fruit. 2022;
XIV. Ralte L, Bhardwaj U, Singh YT. Heliyon Traditionally used edible Solanaceae plants of Mizoram , India have high antioxidant and antimicrobial potential for effective phytopharmaceutical and nutraceutical formulations. Heliyon [Internet]. 2021;7(May):e07907. Available from: https://doi.org/10.1016/j.heliyon.2021.e07907
XV. Boonsombat J, Chawengrum P, Mahidol C, Ruchirawat S, Thongnest S. A new 22 , 26- seco physalin steroid from Physalis angulata. Nat Prod Res [Internet]. 2019;0(0):1–8. Available from: https://doi.org/10.1080/14786419.2018.1550766
XVI. Sun C, Nie X, Kang N, Zhao F, Chen L, Qiu F. A new phenol glycoside from Physalis angulata. Nat Prod Res [Internet]. 2017;6419(January):1–7. Available from: http://dx.doi.org/10.1080/14786419.2016.1269102
XVII. Okmanov RY, Makhmudova MM, Bobaev ID, Tashkhodjaev B. Withanolides from Physalis angulata L . research communications. 2021;804–8.
XVIII. Huong L, Nu T, Duy TN, Thi N, Suong T. Chemical constituents of Physalis angulata L . (family solanaceae). Can Tho Univ J Sci. 2016;2:46–9.
XIX. Filho ER, Pietro RCLR, Kashima S, Sato DN, Janua AH, Franc SC. Antimycobacterial Physalins from Physalis angulata L . (Solanaceae). 2002;448:445–8.
XX. Fitria M, Armandari I, Septhea D, Ikawati A, Meiyanto E. Ekstrak Etanolik Herba Ciplukan (Physalis Angulata L.) Berefek Sitotoksik dan Menginduksi Apoptosis pada Sel Kanker Payudara Mcf-7. Bionatura. 2011;13(2):101–7.
XXI. Chairissy MD, Wulandari LR, Sujuti H. Pro-apoptotic and anti-proliferative effects of. 2019;
XXII. Abbas M, Shahid M, Rehman HM, Sharif S, Muhammad R, Khan A, et al. Screening of Selected Medicinal Plants for Secondary Metabolites. Abstr Accept poster Present in11 Int 23 Natl Chem Conf held NCEPC, Univ Peshawar (October 15-17, 2012). 2012;8(3):119.

XXIII. Baird-Lambert J, Jamieson DD. POSSIBLE MEDIATORS OF THE WRITHING RESPONSE INDUCED BY ACETIC ACID OR PHENYLBENZOQUINONE IN MICE. Clin Exp Pharmacol Physiol. 1983;10:15–20.

XXIV. Wu KK, Ph D. Aspirin and Other Cyclooxygenase Inhibitors : New Therapeutic Insights. Vol. 3, SEMINARS IN VASCULAR MEDICINE. 2003.

XXV. Nicholson B. Responsible prescribing of opioids for the management of chronic pain. Drugs. 2003;63(1):17–32.

XXVI. Conversa G. The good use of NSAID: when, why and how - Pathos [Internet]. 2019 [cited 2022 Oct 31]. Available from: https://www.pathos-journal.com/2019_2_202.html

XXVII. Le H, Anh T, Ba V Le, Do TT, Phan VK, Yen H, et al. Bioactive compounds from Physalis angulata and their anti-inflammatory and cytotoxic activities. J Asian Nat Prod Res [Internet]. 2020;0(0):1–9. Available from: https://doi.org/10.1080/10286020.2020.1825390

XXVIII. Ifora, Arifin H, Silvia R. Efek Antiinflamasi Krim Ekstrak Etanol Daun Kirinyuh (Chromolaena odorata (L) R.M. King & H. Rob) Secara Topikal dan Penentuan Jumlah Sel Leukosit Pada Mencit Putih Jantan. J Farm Higea. 2017;9(1):68–76.

XXIX. 29. Cahyo ASD, Oktavia S, Ifora I. Anti-Inflammatory and Analgesic Potential of Chromolaena odorata: A Review. Int J Pharm Sci Med. 2021;6(9):8–16.

XXX. Wang Y, Chen P, Tang C, Wang Y, Li Y, Zhang H. Antinociceptive and anti-inflammatory activities of extract and two isolated flavonoids of Carthamus tinctorius L. J Ethnopharmacol. 2014;151(2):944–50.

XXXI. Higgs J, Wasowski C, Loscalzo LM, Marder M. In vitro binding affinities of a series of flavonoids for m-opioid receptors. Antinociceptive effect of the synthetic flavonoid 3,3-dibromoflavanone in mice. Neuropharmacology. 2013;72:9–19.

XXXII. Al-Khayri JM, Sahana GR, Nagella P, Joseph B V., Alessa FM, Al-Mssallem MQ. Flavonoids as Potential Anti-Inflammatory Molecules: A Review. Molecules. 2022;27(9).

XXXIII. Rustam M, Ifora I, Fauziah F. Potential Anti-Inflammatory Effects of Eriocitrin: A Review. J Drug Deliv Ther. 2022;12(3):187–92.

XXXIV. González-Trujano ME, Pellicer F, Mena P, Moreno DA, García-Viguera C. Antinociceptive and anti-inflammatory activities of a pomegranate (Punica granatum L.) extract rich in ellagitannins. Int J Food Sci Nutr. 2015;66(4):395–9.