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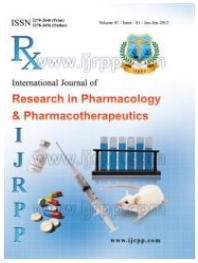

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Analgesic, anti-inflammatory & CNS depressant activity of methanolic extract of plectranthus vettiveroides stem bark in mice

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ABSTRACT

Objectives

This study was conducted to evaluate the analgesic, anti-inflammatory, and central nervous system inhibitory activities of the methanol extract of mouse Platycladus orientalis (MEPV).

Materials and methods

The analgesic activity of MEPV was evaluated by formalin-induced licking and at biting mice with doses of 200 mg/kg and 400 mg/kg body weight. By using the carrageenan-induced inflammation method, the anti-inflammatory effects of MEPV were studied here at doses of 150 mg/kg body weight and 300 mg/kg body weight. CNS inhibitory activity has been measured by generally observing a reduction in exercise doses between 200 and 400 mg/kg body weight in the hole cross assessment.

Results

Statistical analysis showed that compared with diclofenac sodium (79.34%), the 400 mg/kg dose exhibited licking protection (87.30%) in addition to biting formalin-induced rodents in the later stages. Compared with the standard diclofenac sodium (15.94% and 17.48%), the 150 mg/kg dose showed sustained suppression (17.26% and 22.95%) of paw edema at the 3rd and 4th hours. In addition, compared with ordinary diclofenac sodium, the 300 mg/kg dose caused a higher percentage of sustained inhibition of paw edema per hour per hour. In addition, the extract also had a considerable ($p < 0.05$) dose-dependent CNS inhibitory activity.

Conclusion

Current study recommends that this methanolic extract of *Plectranthus vettiveroides* stem bark has important analgesic, anti-inflammatory and CNS depressant properties

Keywords: *Plectranthus vettiveroides,* Analgesic, Anti inflammatory, CNS depressant. GABA

INTRODUCTION

Pain is an unpleasant feeling and emotional experience that is related to tissue damage. Therefore, pain is not perception but feeling [1]. There are several types of pain, including neuropathic pain, nociceptive pain, and psychological pain. Neuropathic pain is due to direct damage to peripheral or central nervous system dysfunction [2]. Nociceptive pain is caused by stimulation of peripheral nerve fibers that only respond to stimuli approaching or

exceeding harmful intensity (nociceptors) [3]. Psychogenic pain is mainly related to disease, and there is no evidence that it may cause pain or its severity [4]. Plants with a history of thousands of years have been used worldwide to control various infectious diseases [5]. Plants as a drug supplier and most developing countries usually use plants as their main drug resources. On a global scale, pharmacists, pharmacologists, microbiologists, biochemists, and botanists are currently studying plants to produce chemicals that can be used to treat various infectious diseases [6].

From the beginning of civilization, medicinal plants have become an important part of human society's fight against diseases (7). In our earliest literature on Ayurveda (Traditional Indian Medicine), Siddha, Unani and Chinese Medicine, there is a lot of herbal knowledge, information and benefits. The World Health Organization reported in 2003 that about 80% of the population in developing countries who cannot afford the cost of medicines rely on traditional medicines (mainly plant medicines) to meet their basic health care needs (8). In developed and developing countries, due to its extensive biological and medical activities, higher safety factors and lower costs, herbal medicines are in great demand for primary health care (9).

Plectranthus vettiveroides is also known as *Coleus vettiveroides*, *Coleus zeylanicus*, *Plectranthus zeynanicus* (Lamiaceae). The main phytochemical components of Iris are diterpenoids, essential oils and phenols. About 140 diterpenes were identified from the colored leaf glands of Platycladus species. The main components of Jerusalem artichoke essential oil are mono and sesquiterpenes. Flavonoids seem to be rare in *Platycladus orientalis*, only two flavonoids have been identified, 4',7-dimethoxy-5,6-cone in *Platycladus orientalis*, thus obtaining viologen from *P.marruboides* And golden chicken essence. Traditionally, it has been used as an antibacterial, deodorant, and cooling agent. It has also been used to prevent headaches and fever from burning eyes. The purpose of this research is to study the antibacterial activity of the stem bark of Phoenix tail.

MATERIALS AND METHODS

Plant Identification and Collection

The plant was collected from Namakkal, Tamil Nadu, India in January 2019. The herbarium specimens of plants are stored in the Pharmacognosy Department. The plant was identified by Dr. G.V.S. Murthy, co-director of the Indian Botanical Survey in the South Ring of Coimbatore TNAU campus, who identified the plant with information he obtained from the literature.

Extraction Procedure

The powdered plant material (bark) weighing 300 gm is loaded into the reagent bottle by using an electronic balance, and then immersed in 700 ml of methanol. Then seal the bottle with cotton swabs and aluminum foil, and keep it for 2 weeks while shaking and stirring from time to time. In addition to Whatman No. 1 filter paper, cotton was used to filter all the mixture. The Buchii rotary evaporator has been used under lower heat and pressure to reduce the volume of the filter. It presents a brown gummy concentrate. The fully focused jelly was designated as the crude extract of methanol. The extract is transferred to a closed tank for further processing.

Animals

Used adult Swiss albinism mice (20-30g) of both sexes that have been produced. Except under standard clinical conditions (the light-dark cycle is 12:12 hours), the temperature is 23ºC±2ºC and the relative humidity is maintained at 55±5%, the five mice are divided into four groups. During the research, they fed standard animal feed and advertising free water.

Chemicals

Diclofenac sodium, ibuprofen and diazepa were purchased from Square Pharmaceuticals Ltd. Physiological saline (0.9%) obtained NaCl from Beximco Infusion Ltd. BDHChemicals Ltd provides Tween80. Formalin, carrageenan and other chemicals are all analytically pure.

Analgesic activity
Formalin-induced hind paw licking in mice

The selected anti-nociceptive activity is usually determined using the formalin test [10]. The control group received 5% formalin. Supervise the methanol extract about the methanol extract of Pseudomonas Vickers stem bark (200 and 400 mg/kg, orally) and diclofenac sodium (10 mg/kg, orally) 60 minutes after supervision, add 20 µl of 5% Forma Lin injected into the back area of the right hind paw). Generally, after the formalin injection, the mice are monitored for 30 minutes, and the time to lick the hind feet of the injection is also noted. The first 5-minute formalin supplement injection is called the early stage, and the period between 15 and 30 minutes is similar to the late stage. Use a stopwatch to observe the total time of licking or biting the injured paw (pain behavior).

Anti Inflammatory action
Carrageenan-induced paw edema in mice

Four groups of mice were conducted for this study, each group containing several mice. Acute inflammation was induced by injecting 0.1 ml (1%) of carrageenan into the flat area of the rat's hind paw. The dose of MEPV (150 and 300 mg/kg), saline (1 ml/kg) and i.p. is (10 mg/kg/i.p) because the referral drug was implemented 30 minutes before the carrageenan injection. The size of the edema was assessed by using a vernier caliper, and the volume of the paw was measured only at 1, 2, 3, and 4 hours. The difference between the readings from the 1 hour time and each time interval is considered the thickness of the edema.

CNS depressant activity
Hole-cross test

The steel partition is fixed in the middle of the crate, the size of the crate is 30×20×14 cm3. A hole with a diameter of 3 cm is made, and the height of the hole is usually 7.5 cm inside the center of the cage. Twenty animals were divided into five tissues, and each group contained four mice. Animals in our group received excipients (1% Tween 80 in normal water, 10 ml/kg, orally), animals in the second group received diazepa at a dose of 1 mg/kg body weight (po), The third and fourth groups were treated with 200 and 400 mg/kg MEPV body weight (po), respectively. About 0, 30, 60, 90 days and 120 minutes after oral analysis of the samples, the number of passages from one chamber to a new chamber was counted in a new period of 3 minutes [11].

RESULTS

Formalin-induced hind paw licking in mice

Table 1 generally shows the results of MEPV against formalin-induced hindfoot licking actions in mice. Biologicals pretreated with MEPV (200 and 400 mg/kg) showed a significant dose-related reduction ($p<0.05$). Hindfoot licking caused by formalin. In particular, MEPV treated at a dose of 400 mg/kg showed better exercise in the late stage compared with the standard (diclofenac sodium 10 mg/kg).

Table 1: Effect of MEPV on hind paw licking in the formalin test in mice.

Groups	Dose (mg/kg)	Early phase	% of inhibition	Late phase	% of inhibition
Group I (control)	Vehicle	28 ± 4.12	-	23.79 ± 1.26	-
Group II (Standard)	Diclofenac Sodium 10	8 ± 1.02*	58.28	4.41 ± 0.26*	79.34
Group III	200	17 ± 0.70*	36.94	8.31 ± 0.21*	63.08
Group IV	400	11 ± 0.68*	43.61	4.51 ± 2.46*	87.30

Values are mean (n=5) ± SEM (standard error mean) '* ' denotes p<0.05, compared with vehicle control (one way ANOVA followed by Dunnet's test).

Carrageenan-induced paw edema in mice

Figure 1 shows the effect of MEPV on carrageenan-induced edema. MEPV exerted a new and important anti-inflammatory effect at typical doses of 150 and 300 mg/kg ($p<0.05$), which was comparable to the typical control group. In the 4th hour of standard consumption, in addition to the standard (ibuprofen) 10 mg/kg, the inhibition percentages of MEPV (150 and 300 mg/kg) were 21.83%, 22.56% and 17.36%, respectively.

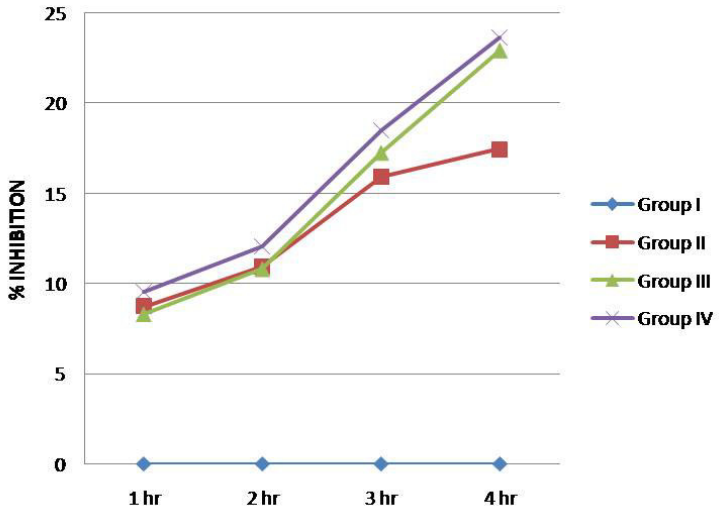

Figure 1: Anti-inflammatory Activity of MEPV.

CNS Depressant action

Hole-cross test

Table 2 provides the results of the hole crossing test of MEPV. For almost all dose ranges at 30, 60, and 90 minutes, they are statistically significant and follow a dose-dependent response. Generally, the inhibitory effect is most obvious when the dose is 400 mg/kg.

Table 3: Effect of MEPV on hole cross test in mice.

Groups	Dose (mg/kg)	Number of movements				
		0 min	30 min	60 min	90 min	120 min
Group I	Vehicle	7.19 ± 0.75	7.99 ± 1.03	6.79 ± 0.75	6.59 ± 0.40	6.18 ± 0.23
Group II	Diazepam 1 mg	2.79 ± 0.55*	2.59 ± 1.07*	1.19 ± 0.86*	1.09 ± 0.72*	0.54 ± 0.26*
Group III	200 mg	5.19 ± 0.48	4.59 ± 0.40	3.70 ± 0.26*	2.53 ± 0.70*	1.43 ± 0.26*
Group IV	400 mg	1.19 ± 0.47*	1.39 ± 0.50*	1.08 ± 0.45*	0.79 ± 0.70*	0.69 ± 0.55*

Values are mean (n=5) ± SEM (standard error mean) '* ' denotes p<0.05, compared with vehicle control (one way ANOVA followed by Dunnet's test).

DISCUSSION

The formalin test may be an important model of analgesics and has a better relationship with clinical pain [12]. Nociception caused by formalin is biphasic, with the first stage involving direct stimulation of sensory nerve fibers that resolve neuropathic pain. The second stage of formalin-induced nociception involves inflammatory pain. In addition to NO, it is also composed of prostaglandin, serotonin, histamine, Bradikinin and IL-1β, IL-6, TNF-α, eicosanoid Mediated by other cytokines [13-18].

MEPV showed an inhibitory effect on the second nociception induced by formalin in mice, and the inhibitory effect was higher than that of typical diclofenac sodium. By simply reducing the hyperalgesia caused by bradykinin and cytokines (TNF-α, IL-1β) and the release of IL-1β and PGE2 in the paw skin activated by polysaccharides, MEPV can be determined to have analgesic effects. In addition, compared with standard diclofenac sodium, in addition to bite-induced mice, the extract usually at a dose of (400 mg/kg) also has a greater anti-licking effect. In this test, the usual inhibition of the licking response from the late MEPV indicates the analgesic effect of the typical formalin test associated with the extract.

Foot edema caused by carrageenan continues to be widely used as an experimental animal model for acute irritation. It is considered to be biphasic, in which the early stage (1-2) of the carrageenan model is mainly mediated by histamine and serotonin. In addition, the synthesis of prostaglandin in the surrounding environment of the damaged tissue increases, and the overdue stage is simple Maintenance is mediated by the release of prostaglandins and the prostaglandins produced by bradykinin, leukotrienes, polymorpho nuclear cells and tissue macrophages [19]. In this study, although the standard indomethacin indicated a relatively low percentage of inhibition, 300 mg/kg crude MEPV showed considerable paw edema at 1, 2, 3, and 4 hours. In addition, the removal of crude methanol except MEPV at a dose of 150 mg/kg also showed significant and sustained foot edema inhibitory effects on the 3rd day and the 4th hour. Generally, the commonly observed possible mechanism of anti-inflammatory activity may be its ability to reduce the release of histamine, this or kinin-like substance, or even the biosynthesis ability of prostaglandins, which is consistent with the analysis of analgesic activity.

Plant extracts have key nervous system inhibitory activities, as indicated by the decline in mice's exploratory behavior. In addition, exercise studies, usually measured by gap crossing tests, show that the composition of the leaves (200 mg/kg and 400 mg/kg) reduces the frequency and amplitude of exercise. Since motor activity is actually related to the level of central nervous system excitability [20], the reduction in intrinsic spontaneous motor activity can be attributed to the sedative effect of specific plant extracts [21, 22].

Different anti-anxiety drugs, muscle relaxants and sedative hypnotic drugs explain their effects through GABA, so it can be achieved that pineapple extract can simply enhance the GABAergic inhibitory effect in the CNS through membrane hyperpolarization, thereby reducing cortical nerves Yuan's injection rate. It may be due to the direct effect of brain extracts on GABA receptors [23].

CONCLUSION: *Plectranthus vettiveroides*

The bark of *Plectranthus vettiveroides* extract has impressive anti-injury, anti-inflammatory and central nervous system inhibitory activities. The current function is a preliminary work that usually requires further detailed exploration, including the characterization of high-energy compounds and pre-formulation research for the development of potential dosage forms.

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