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RESEARCH ARTICLE

ANTINOCICEPTIVE ACTIVITY OF METHANOLIC EXTRACT OF THE RHIZOMES OF *HEDYCHIUM CORONARIUM*

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ABSTRACT

The study is based on the investigation of antinociceptive activity observed from the methanolic extract of the rhizomes of *Hedychium coronarium*. Tail immersion method in mice has been used for the evaluation of the central pharmacological actions. Similarly acetic-acid induced writhing-test was used for the evaluation of the peripheral pharmacological properties. A substantial rise in pain threshold is seen in a dose dependent manner with the methanolic extract of the rhizomes of *H. coronarium* at doses of 50, 100 and 150 mg/kg body weight with the tail immersion methods. The methanolic extract at 150 mg/kg dose possessed 82% writhing inhibition, (p <0.001) in acetic-acid induced writhing-test that could be compared to the standard, Diclofenac-Na (25 mg/kg) with76% inhibition. Hence, the above results evidence the presence of antinociceptive properties of the rhizomes of *H. coronarium.*

INTRODUCTION

Hedychium coronarium belongs to the family Zingiberaceae known with many common names as cinnamon jasmine, ginger lily, butterfly lily, garland flower and butterfly ginger. In India, it is known as "gandasuli" which means "the fragrance of princess" in Sanskrit, with the rhizomes playing an important role in folk remedy. It is known to be widely cultivated in Asian countries such as India, South China, Taiwan, Japan and also in Brazil. The widespread use of the rhizome of *H. coronarium* is seen in the Chinese natural medicine for the treatment of pain due to rheumatism, headache, contusion inflammatory and lancinating pain while in the Indian Ayurvedic medicine, it is used for the treatment as an excitant, anti-rheumatic, tonic and febrifuge (Matsuda *et al.,* 2002). Previously in *Hedychium* genusditerpenoids (Suresh *et al.,* 2010; Reddy *et al.,* 2009; Reddy *et al.,* 2010) flavonoids (Rao *et al.,* 2009, 2012), oxygenated sesquiterpenoids (Suresh *et al.,* 2010) and chalcones (Rao *et al.,* 2012) were reported. Essential oils, extracts and their constituents of plants are greatly valued in ayurveda and have also been reported to exhibit a wide range of biological activities (Suresh, *et al.,* 2010; Reddy *et al.,* 2008, 2009; Reddy *et al.,* 2010; Rao *et al.,* 2009, 2012) which are of therapeutic importance that include antiseptic activity, antimicrobial, osteoarthritis of the knee, antitumor (Reddy *et al.,* 2010), antiulcer, diabetes (Reddy *et al.,* 2009), anthelmintic activity, certain heart problems, central nervous system disorders (White *et al.,* 2014, 2015), gastrointestinal disorders (Salaga *et al.,* 2014), Most of the diterpenoids, flavonoids and their analogs play an important role in the drug discovery (Fajemiroye *et al.,* 2014; Aktar *et al.,* 2008, Raju *et al.,* 2008; Polepally *et al.,* 2012, 2013, 2014).

The rhizomes of *Hedychium coronarium*, which have a strong aromatic odour, is a well-known crude drug used as an aromatic stomachic in China and India. Pain, an unpleasant emotional and sensory experience, is often related to potential damage of tissues. Pain is known to have a proactive function against the disturbances of the body that bring the patients to physician. The common drugs used against pain are analgesics as NSAIDs or opiates that could relieve the symptoms, with no effect to its cause (Salaga *et al.,* 2014; Zjawiony *et al.,* 2011).But these analgesics could not always be considered for the treatment of pain due to their adverse effects and hence there is the need for new compounds with fewer side-effects and better pain-management. In present study, we investigated the antinociceptive activities of methanolic extracts of the rhizomes of *H. coronarium*.

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MATERIALS AND METHODS

Plant material

Fresh rhizomes of *H. coronarium* were collected from the garden of the Regional Research Laboratory, Thiruvanathapuram, India. Collected rhizomes of *H. coronarium* were cut into small pieces, dried and pulverized into a coarse powder and stored in an air-tight container.

Extraction and sample preparation

The pulverized coarse powder of rhizomes of *H. coronarium* (250 gm) was extracted with methanol at least three times by successive cold extraction. The extracts obtained, were filtered off and evaporated to dryness in an oven at low temperature. The extracts rendered concentrate of brownish colour.

Animals

For the experiments, both male and female Swiss albino mice, 3-4 weeks of age, weighing between 20-25 gm, were collected from the animal research branch of the National Center of Animals and Research (NCAR), Odisha. Animals were maintained under standard environmental conditions (temperature: (24±2^{o}C), relative humidity: 55-65% and 12 hrs light/12 hrs dark cycle) and had free access to food and water ad libitum. The animals were acclimatized to laboratory conditions for one week prior to experimentation.

Antinociceptive activity

Tail immersion test

The procedure is based on the observation that morphine like drugs selectively prolongs the reaction time of the typical tail withdrawal reflex in mice. The animals were treated as mentioned above and 1 to 2 cm of the tail of mice was immersed in warm water keeping constant at 55°C. The reaction time is calculated as the time taken by the mice to deflect their tails.

The first reading was omitted and then the reaction time was recorded as a mean of the following three readings. Complete analgesia is the latency period of 12s and the measurement was then stopped to avoid further injury to the mice. The latent period of the tail-flick response was determined at intervals of 0, 30, 60 and 90 min following the administration of drugs (Salaga *et al.,* 2014). Percentage of elongation was calculated using the following formula.

$$\text{Elongation (\%)} = \frac{\text{Latency (Test) - Latency (Control)}}{\text{Latency (Test)}} \times 100$$

Acetic Acid-Induced Writhing Test

The analgesic activity of the samples was also studied using acetic acid-induced writhing model in mice. Test samples and Control were administered orally, 30 min before intraperitoneal administration of 0.7% acetic acid but Diclofenac-Na was intra-peritoneally administered 15 min prior to injection of acetic acid where Diclofenac- Na (25mg/kg) was used as a standard. After an interval of 5 min, the mice were observed for specific contractions of the body referred to as 'writhings' for the next 10 min.[22] Percentage inhibition of writhing was calculated using the following formula:

$$\text{Writhing inhibition (\%)} = \frac{\text{Mean No. of writhing (control) - Mean No. of writhing (test)}}{\text{Mean No. of writhing (control)}} \times 100$$

Statistical Analysis

Statistical analysis for animal experiments was carried out using one-way ANOVA followed by Dunnett's multiple-comparisons. The obtained results were comparable with the vehicle control group. p values < 0.05 and 0.001 were considered to be significant statistically.

RESULTS

The analgesic activity of the methanolic extract of *H. coronarium* was evaluated using tail immersion and acetic

Table 1. Effects of the Methanolic Extract of *H. coronarium* on tail withdrawal reflex of mice induced by Tail immersion method

Groups	Dose (mg/kg)	Mean reaction time(s) before and after drug administration (% of tail flick elongation)			
		0 min	30 min	60 min	90 min
Control		1.73 ±0.125	1.60±0.125(-)	1.47±0.17 (-)	1.33±0.105 (-)
Standard (Diclofenac-Na)	25	2.53±0.29	5.33±0.235** (69.98%)	7.39±0.07 ** (80.10%)	8.8±0.17**(84.88%)
Group – I	50	1.82±0.02	4.45±0.385 (64.04%)	6.09± 0.405**(75.86%)	7.06±0.50** (81.16%)
Group – II	100	1.86±0.035	5.53±0.335** (71.06%)	6.28 ±0.495** (76.59%)	7.44±0.305** (82.12%)
Group – III	150	1.82±0.05	6.50±0.24** (75.68%)	7.38±0.325** (80.08%)	9.88±0.495** (86.53%)

Control: animals received (1% Tween 80in water), Standard group received Diclofenac–Na (25 mg/kg body weight i.p.), Group-I, Group-II and Group – III were treated with 50, 100 and 150 mg/kg body-weight of the extract per oral. Values are mean ±SEM, (n=4);
**p <0.001, Dunnett's test as compared to control

Table 2. Effect of *H. coronarium* Methanolic Extract on Acetic Acid induced writhing in Mice

Group	Treatment and Dose	Writhing (Mean ±SEM)	% of writhing	% of writhing inhibition
Control	0.7% acetic acid (10ml/ kg, i.p.)	41.3±1.32	100.00	0
Standard	Diclofenac sodium (25 mg/kg i.p.)	10.0±0.42**	24.21	75.78
Group – I	Extract (100 mg/kg per oral)	30.5±1.035**	73.85	26.15
Group – II	Extract (200 mg/ kg per oral)	21.5±0.995**	52.06	47.94
Group – III	Extract (400 mg/ kg per oral)	11.1±2.88**	26.87	73.12

Diclofenac sodium was administered 15 min before 0.7% acetic acid administration. Writhing was counted for 15 min, starting after 5 min of acetic acid administration; **p<0.001 vs. control, values are mean ±SEM; (n=5)

acid-induced writhing methods. The tail withdrawal reflex time following the administration of the extract of *H. coronarium* was found to escalate as the sample-doses were increased. The maximum effect was seen subsequently with the administration of the drug at 60 and 90 min. The results were significant statistically ($p<0.05$-0.001) and were comparable to the control (Table 1). The doses of *H. coronarium* extract significantly ($p < 0.001$) inhibited the writhing responses induced by acetic acid in a dose dependent manner as compared to the control. At 100 mg/kg body weight the extract showed 26.15% inhibition, at 200 mg/kg body weight the extract showed 47.94% inhibition and at 400 mg/kg body weight showed 73.12% inhibition of writhing compared to the standard drug Diclofenac-Na which showed 75.78% inhibition of writhing at 25 mg/kg body weight dose (Table 2).

DISCUSSION

Acetic acid induced writhing test is suitable for detecting both central and peripheral analgesia, whereas tail flick tests are most sensitive to centrally acting analgesics. Intraperitoneal administration of acetic acid releases prostaglandins and sympathomimetic mediators like PGE2 and PGF2α and their levels increase in the peritoneal fluid of the acetic acid induced mice. The abdominal constrictions that are produced following the administration of acetic acid is related to the sensitization of the nociceptive receptors to prostaglandins. It is thus possible that the *H. coronarium* extract exerts its analgesic effect by preventing the synthesis or action of prostaglandins that may be due to the phytochemicals present in the extract. Induction of nociception thermally, indicates the narcotic involvement. In general, the centrally acting analgesics elevate the pain threshold of mice towards heat. In tail flick method, the *H. coronarium* extract significantly delayed the response time to the thermal pain sensation indicating narcotic involvement. Moreover, the inhibition of both peripheral and central mechanisms of pain by the extract indicates its action on opioid receptors.[10-21, 23] Results of the present investigation suggest that the extract of *H. coronarium* possesses strong analgesic activity and provide a scientific basis for the use of the plant in traditional system of medicine in the treatment of inflammatory disorders.

Conclusion

From the above results, it could be concluded that the plant extract of *H. coronarium* is known to possess significant antinociceptive properties that could be mediated from the depression in the central mechanism of pain, enhancing the support of the plant for use in pain and inflammatory-disorders. However, it is essential to study further to understand the exact mechanisms underlying in the compound(s) yet to be isolated that could be responsible for the antinociceptive properties.

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