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ANTI-NOCICEPTIVE EFFECT OF ALCOHOLIC AND AQUEOUS EXTRACTS OF *AEGICERAS CORNICULATUM*

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ABSTRACT

In this study anti-nociceptive effects of ethanolic and aqueous extracts of Aegiceras corniculatum leaves belonging to family Primulaceae were studied in. Preliminary phytochemical screening revealed the presence of various vital components. The extract was found to be nontoxic upto the dose of 2000mg/kg. The ethanolic and aqueous extracts of Aegiceras corniculatum (200 and 400 mg/kg , p.o) produced significant analgesic effect, extended latency period in Eddys hot plate and decreased the number of writhing induced by acetic acid in a dose dependent manner.

INTRODUCTION:

Pain is the most common reason people seek medical attention. It can be defined simply as an undesirable physical or emotional experience and it can be classified as acute or chronic. Treatment for chronic pain is a major public health problem due to the recurrent use of available drugs that have undesirable side effect [1]. For thousands of years, various forms of natural products have been used for treating pain disorders, such as the use of opium, extracted from Papaver soniferum L. From the nineteenth century; bioactive compounds began to be isolated and identified. Then, the action of such molecules was enhanced, such as salicin, a compound extracted from the bark of the white willow tree (Salix alba L.), from which the acetylsalicylic acid is produced [2]. Whereas morphine remains as the most potent analgesic drug, which was first isolated in 1803 by Friedrich Sertürner [3]. Research in pain management and drug addiction are focused on natural products. Analog compounds have been produced from natural substances, and synthetic compounds based totally on natural pharmacophores have been introduced in the market [2]. There are various forms of analgesics that contribute to reducing pain. They are classified into three categories: opioid analgesics (e. g. morphine and codeine); non-opioid analgesics, such as nonsteroidal anti-inflammatory drugs (NSAIDs) among which stands out aspirin and diclofenac; and adjuvant analgesics, which are compounds commonly administered for other reasons than pain, but can control it in certain situations. Antidepressant medications can act as analgesics in the treatment of many chronic pain states. Opioid analgesics cause a maximal analgesia; they are considered broad- spectrum drugs in the treatments of acute pain because of their great efficacy [4]. However, the clinical use of these drugs suffers from disadvantages because they have adverse effects such as hypertension, hyperglycemia, increased susceptibility to infection, osteoporosis, and cardiovascular disease, among others [5]

The plant-based preparations are commonly used, but the real effectiveness and the relevant active ingredients are often unknown. Nevertheless, they are drugs and as such, they have drawbacks and side effects if they are not properly administered. For these reasons, it is interesting to determine whether the use of a plant that has been applied as a medicine is supported by real pharmacological effects [7].

The goal of any analgesic property test is to find any analgesic particle in the plant crude extracts. Pain is probably the most prevalent symptom in clinical practice, and characterization of pain is of major importance in the diagnosis and choice of treatment [11]. In the treatment of diseases associated with pain, the clinical effects typically guide the selection of the analgesics and titration of the dose. However, in practice, the different symptoms of the underlying diseases confound the characterization of pain. These confounders may include complaints relating to psychological, cognitive and social aspects of the illness, as well as systemic reactions such as fever and general malaise [12].

MATERIALS AND METHODS:

Preparation of extracts

Aegiceras corniculatum was collected from kanniyakumari district, tamilnadu, India. The aerial parts of the plant was dried under shade and extracted with 90% ethanol and water by hot soxhlet method.

Experimental animals

Albino mice weighing 20–25 g and young adult Wistar rats of both sexes weighing 150–200 g were used. The animals were kept and maintained under laboratory conditions of temperature, humidity and light; and were allowed free access to food (standard pellet diet) and water ad libitum. The animals were divided into plant extract- and drug-treated ‘test’, and distilled water-treated ‘control’ groups of eight animals per group. All the animals were fasted for 16 h, but still allowed free access to water, before the commencement of the experiments. The mice were used for assessment of acute toxicity testing and analgesic activity of extracts.

Acute toxicity studies.

Albino mice weighing 22–25 g (three female animals) were used in the study. Acute oral toxicity was performed as per the OECD-423 guidelines4.The animals were fasted overnight, provided with water after which EEAC and AEAC was administered orally. The animals were observed for toxic symptoms such as behavioral changes, locomotion, convulsions and mortality.

Grouping of animals

Each group was allotted six animals each. Group I: Received 3% aqueous suspension of gum acacia (1ml/200g) as vehicle, Group II: Received paracetamol (PAL) standard drug, Group III: Received EEAC (200 mg/kg), and Group IV: Received EEAC (400 mg/kg). Group V: Received AEAC (200 mg/kg), and Group VI: Received AEAC (400 mg/kg).

Acetic acid test method

Analgesic activity was evaluated in mice using the writhing test8. Mice were given an intraperitoneal injection of 0.7% (v/v) aceticacid solution (volume of injection was 0.1 ml/10 g body weight). Paracetamol at a dose of 45mg/kg was used as standard. The number of writhes produced in these animals was counted for 20 min.

Hot-plate test method

Analgesic effect was further evaluated using hot plate method described by Eddy 9. The hot plate was maintained at 55±0.50C. The animals which showed pain response to the hot plate were selected. The standing time on the plate was limited to 10sec to avoid damage to the paws of the animals. The number of jumping and paw licking was assessed.

Table 1. Anti-nociceptive activity of ethanolic extracts of Aegiceras corniculatum: Acetic acid test method

Treatment	Number of writhings in 20 mins	Inhibition %
Control	41.36 ± 4.40	0.00
Paracetamol (100mg/kg)	2.60 ± 1.10**	93.86**
EEAC (200mg/kg)	22.44 ± 4.39*	51.75*
EEAC (400mg/kg)	12.89 ± 3.45*	74.29*
AEAC (200mg/kg)	20.55 ±3.26*	50.31*
AEAC (400mg/kg)	14.78± 2.69*	64.26*

Each value represents mean ±SEM of 6 observations. *p < 0.05, **p<0.001 vs control. Data was analyzed by student's t test. One-way ANOVA followed by Dunnett's test

Statistical analysis

The data represent mean ± SEM. The results were analyzed statistically using one-way ANOVA followed by Dunnett's test. The minimum level of significance was set at $p < 0.05$. All assays were conducted in triplicate and statistical analysis was done, using Graph pad Prism (version 5) software.

RESULTS AND DISCUSSION

Acute toxicity studies

The EEAC and AEAC did not produce any toxic symptom or mortality up to a dose level of 600mg/kg body weight orally in mice, and hence the drugs were considered safe for further pharmacological screening. According to OECD-423 guidelines for acute oral toxicity, a LD50 dose of 2000 mg/kg and above is categorized as unclassified.

Acetic acid test method

Table 3 shows the effect of EEPV and AEAC on acetic acid induced writhing. Treatment with PAL showed significant (P<0.001) reduction in number of writhes when compared with control. EEMP 200 and 400 mg/kg and AEAC 200 and 400 mg/kg also showed significant (P<0.05) percentage inhibition of writhes when compared with control.

Table 2. Anti-nociceptive activity of ethanolic extracts of Aegiceras corniculatum :Hot-plate test method

Treatment	Mean reaction time	Protection %
Control	10.31 ± 1.41	0.00
Paracetamol (100mg/kg)	20.28 ± 1.43**	92.95**
EEAC (200mg/kg)	14.50 ± 1.43*	41.95*
EEAC (400mg/kg)	16.01 ± 1.40*	65.10*
AEAC (200mg/kg)	12.76 ± 1.26*	23.76*
AEAC (400mg/kg)	15.57 ± 1.35*	51.01*

Each value represents mean ±SEM of 6 observations. *p < 0.05, **p<0.001 vs control. Data was analyzed by student's t test. One-way ANOVA followed by Dunnett's test

Hot-plate test method

Table 4 shows the effect of EEPV and AEAC on Eddy's hot plate. Treatment with PAL showed significant (P<0.001) protection and increased the mean reaction time when compared with control. EEMP 200 and 400 mg/kg and AEAC 200 and 400 mg/kg also showed significant (P<0.05) percentage protection when compared with control.

CONCLUSION

In acute toxicity study, oral administration of Aegiceras corniculatum did not produce any mortality in mice upta dose level of 2 g/kg. This may be due to the broad non-toxic range of the plant. The results of the present study revealed the analgesic effect of Aegiceras corniculatum leaves. Acetic acid induced writhing and eddys hot plate test to thermal stimulation are models of pain that mainly involve peripheral and central mechanisms respectively. Analgesic effect observed in both these experiments with EEAC and AEAC indicates the involvement of both peripheral and central mechanisms. Tannins and flavonoids have shown to possess

analgesic effect. Aegiceras corniculatum was found to have tannins and flavonoids [14] which may further contribute to the analgesic effect of Aegiceras corniculatum. As EEAC and AEAC showed a dose dependent response on analgesic activity. The present study demonstrates the potential anti-nociceptive effects of Aegiceras corniculatum, which supports the folklore claims as an analgesic remedy.

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