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Research Article

INVESTIGATING ANTI NOCICEPTIVE ACTIVITY OF *POLYCARPAEA CORYMBOSA* LAM. (CARYOPHYLLACEAE) IN STANDARD EXPERIMENTAL ANIMAL

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ABSTRACT

Objective: *Polycarpaea corymbosa* Lam. is traditionally used to treat inflammation and jaundice. The aim of the present study was to evaluate the Analgesic activity

Method: The model used was Eddy's hot plate method and Tail flick method in which the animals treated with *Polycarpaea corymbosa* and standard drug Pentazocin has significantly increased the latency period of jumping & paw licking when compared with control group animals.

Result: The methanolic aerial extract of *Polycarpaea corymbosa* at a dose of 200 mg/kg b.wt. has shown significant analgesic activity than root. The results indicated that the analgesic effect of *Polycarpaea corymbosa* methanolic extract is both peripherally and centrally significant.

Conclusion: Results are highly promising and ascertain that aerial part of *P.corymbosa* have analgesic, comparable to that of standard drug Pentazocin. The findings indicated the analgesic activity of the aerial and root of the plant acting both centrally and peripherally.

Keywords: *Polycarpaea corymbosa* Lam., Analgesics activity, Eddy's hot plate, Tail flick method, Pentazocin.

INTRODUCTION

Man's existence on earth has been made possible only because of the vital role played by the plants in sustaining life .Medicinal plants are believed to be an important source of new chemical substances with potential therapeutic effects [1]. Plants are the basis for traditional medicine systems and used for thousands of year in countries such as India and China. Numbers of medicinal plants and its derived extracts are used in the treatment of various disorders by Ayurveda, Unani and Siddha systems in India. Scientifically, few of pharmacological properties has been studied to supports its traditional use [2]. Substances such as alkaloids, flavonoids and terpenoids synthesized from plants have recently been discovered to have commendable analgesic properties [3].

Pain is in general seen as nociceptive, inflammatory or a neuropathic response. Pain is primarily managed with analgesics. Opioid analgesics are commonly used for treatment of pain. Although opioids are strong analgesics, there are other drugs used for the treatment of pain. Antidepressants and antiepileptics are also used in pain management [4]. In analysis the research during the last decades, it is estimated that the analgesics are one of the highest therapeutic categories on which research efforts are concentrated [5]. Analgesic compounds available in the market, still present a wide range of undesired effects [6] leaving an open door for new and better compounds. Natural products are believed to be an important source of new chemical substance with potential therapeutic applicability [7].

Polycarpaea corymbosa Lam. is a herb of annual or perennial, with taproots slender to stout, stems erect, branched, terete, leaves opposite, sometimes appearing whorled belonging to the family Caryophyllaceae. Flavonoids and phenolic compounds widely distributed in plants have been reported to exert multiple biological effects, including antioxidant [8], anti-inflammatory, anticarcinogenic, etc. Leaves, flower heads of *P.corymbosa* are used in reducing fever; anti-inflammatory and as a poultice for boils and other swellings; antidote for snakebite, leaves were reported to posses potent antioxidant property and are used for treatments of jaundice, demulcent and astringent in Indian folk medicine. The whole parts of *P.corymbosa* are used in Indian traditional medicinal system in inflammatory swellings and in treatment of ulcer, jaundice [9]. The current literature survey revealed that there is no scientific documentation on aerial parts of *P.corymbosa* for its analgesic activity to support its traditional use.

MATERIALS AND METHODS

Plant materials collection and identification

Polycarpaea corymbosa Lam. (Caryophyllaceae) were collected from Chennimalai, Erode dist., Tamil Nadu, India. The specimen was authenticated at Botanical Survey of India (No. BSI SCR 5/23/2011-12 Tech.1391), Coimbatore and is documented in our laboratory. The shade dried, powdered aerial and root parts were stored in air-tight container.

Extraction of plant material

The powdered aerial and root of the plant (50g) was exhaustively extracted with methanol using soxhlet apparatus for 72 h. The extract was concentrated under reduced pressure using rotary evaporator and stored at 2˚C - 8 ˚C until the completion of pharmacological studies. The yield of extract was noted (21.62 and 32.6 % w/w for aerial and root respectively).

Animals

Swiss mice weighing 20-25 g were used throughout this study. The animals were randomly housed in appropriate cages at 21-23˚C on a 12h light/dark cycle with free access to food and water *ad libitum*. The experimental protocols were approved by institutional Animal Ethical Committee (Reference no. 659/02/a/CPCSEA).

Toxicity Study

Acute oral toxicity study was performed as per OECD-423 guidelines [10]. Swiss albino mice (n =6) of either sex selected by random sampling technique were used for the study. The animals were kept fasting for overnight providing only water, after which the aerial and root extracts were administered orally at the dose level of 5mg/kg body weight (1000, 2000, 3000, 4000 and 5000mg/kg b.wt.) by oral feeding needle and observed for 14 days. Mortality was not observed at 2000 mg/kg body weight which was considered as LD_{50} cut off dose (11).

Experimental design

Grouping: Swiss mice weighing between 20- 25 gms were divided into 4 groups of 6 mice each; three animals being housed in a labelled cage each. Animals were given a period of time to adjust to the new environment provided with food & water *ad libitum*.

Group I: Animals were administered 0.1ml saline p.o

Group II: Animals were administered standard reference Pentazocin (30 mg/kg b.wt.) i.p.

Group III: Animals were administered Aerial methanolic extract of *P.corymbosa* (200 mg/g b.wt.) p.o

Group IV: Animals were administered Root methanolic extract of *P.corymbosa* (200 mg/g b.wt.) p.o

Hot plate method

Experimental animals of either sex were randomly selected and divided into three groups designated as group-I, group-II and group-III consisting of six mice in each group for control, positive control and test sample group respectively. Each group received a particular treatment i.e. control (0.1 ml saline), positive control (Pentazocine 30 mg/kg b.wt., p.o.) and the test samples (methanolic aerial and root extract of 200 mg/kg b.wt., p.o.). The animals were positioned on Eddy's hot plate kept at a temperature of 55±0.5 ˚C. A cut off period of 15 s [12] was observed to avoid damage to the paw. Reaction time was recorded when animals licked their fore or hind paws, or jumped prior to and 0, 30, 60, 90, 120, 180 and 210 min after oral administration of the samples [13,14].

Tail-Flick Model

The central analgesic activity was determined by radiant heat tail-flick model in mice [15]. The analgesic activity of the plant extract was studied by measuring drug induced changes in the sensitivity of the prescreened mice (the intensity of the light beam has been experimentally defined such that naive animals will withdraw their tails within 2 to 4 s) to heat stress applied to their tails by using analgesiometer. Basal reaction time of radiant heat was taken by placing the tip (last 2 cm) of the tail on the radiant heat source. Tail withdrawal from the heat (flicking response) was taken as the end point. A cut off period of 10 sec was observed to prevent damage to the tail. The tail flick latencies were recorded at pre-drug, 15, 30, 45, 60 and 75 min after administration of vehicle or drugs. Methanol aerial and root extract of *P.corymbosa* (200 mg/kg b.wt.) was used as the test drug. Pentazocine 30 mg/kg b.wt., was taken as standard drug.

Statistical analysis

All the data's were analyzed using One-Way ANOVA method followed by Dunnet's / Tukey's test. All values were reported as mean SEM. P≤0.05 was considered to be statistically significant.

RESULTS AND DISCUSSION

The OECD guideline 423 fixed dose methods study showed that extract was safe at a dose of 200 mg/g b.wt. The mehanolic extract of *P.corymbosa* aerial at a dose of 200 mg/kg b.wt. has shown significant analgesic activity as compared to root extract. The analgesic activity of root of *P.corymbosa* was studied for its central activity. The reaction time (paw licking / jumping response) in rats in hot plate method, pretreated with aerial and root dose of *P.corymbosa* (200mg/kg b.wt.) and Pentazocine (30 mg/kg b.wt.) at 60, 90 min were found to be 3.1±0.2, 2.8±0.61, 2.7±0.36 and 2.49±0.3, 2.35±0.47, 2.16±0.47 respectively, when compared to control group mice (Table 1). The percentage increase in the reaction time caused by the extract and Pentazocine was detectable and peaked, at +1 h and +30 min respectively but thereafter declined relatively at +3h after the administration of the extract. The results of tail flick test indicated a significant increase in reaction time at 45 and 75 minutes with 200 mg/kg of methanolic extract of *P.corymbosa* whereas reference drug pentazocin significantly increased the reaction time at 30 to 75 minutes (Table 2).

Table 1: Results of methanolic aerial and root extract of *P.corymbosa* by Hot Plate reaction time in mice.

Groups	Dose(mg/kg)	Reaction time (seconds)						
		Initial	Time after drug administration (mins)					
			30	60	90	120	150	180	210
I	-	3.5±0.76	3.5±0.76	2.5±0.42	2±0.26	3.5±0.42	5.5±0.42	5±0.36	4.5±0.42
II	30	5.66±0.42	5.83±0.47	5±0.57	4.5±0.42	5.5±0.61	6.3±0.49	6.33±0.42	5.56±0.66
III	200	3.16±0.47*	3.6±0.61	3.4±0.57**	3.3±0.36**	3.3±0.22*	3.1±0.42*	2.8±0.61	2.7±0.36
IV	200	3±0.68***	3.66±0.33**	3.5±0.42*	2.76±0.3*	2.66±0.49**	2.49±0.3*	2.35±0.47*	2.16±0.47**

Values are given as Mean ± SEM for groups of six animals each.

*P<0.05, **P<0.01 and *** P<0.001 as compared to positive control vs extracts, Control rats and drug treated rats.

Analgesics are primary need of patients to get rid of any kind of pain. The pain is one of the basic symptoms of almost all human ailments which are a sensorial modality and primary protection. Analgesics only relieve pain in a particular complaint without affecting its cause [16]. The most eminent analgesics including opiates and NSAIDs are not helpful in all cases due to their adverse effects. Consequently, the new compounds with potent painkiller action and no side effects are being required to investigate. The analgesic activities of many plants have been attributed to their terpenoids and flavonoids contents [17].The present study establishes the analgesic activities of the methanolic extract of *P.corymbosa* using the hot plate method and tail flick method in mice. The hot plate method is useful in detecting centrally acting analgesics [18]. The hot plate test measures the complex response to a non-inflammatory, acute nociceptive input and is one of the models normally used for studying central nociceptive activity [19]. It is an established fact that any agent that causes a prolongation of the hot plate latency using this test must be acting centrally [20]. The tail-flick response is believed to be a spinally mediated reflex and the paw-licking hot plate response is more complex supraspinally organized behavior [21]. The effectiveness of analgesic agents in the tail-flick pain model is highly correlated with relief of human pain perception (22). Therefore, the methanolic extract of *P.corymbosa* must have a central activity. Again, narcotic analgesics inhibit both peripheral and central mechanism of pain, while NSAIDs inhibit only peripheral pain [23,24].

Table 2: Results of methanolic aerial and root extract of *P.corymbosa* by tail flick method.

Groups	Dose(mg/kg)	Reaction time (seconds)					
		Initial	Time after drug administration (mins)				
			15	30	45	60	75
I	-	3.66±0.49	3.83±0.3	4±0.57	3.16±0.47	3.5±0.42	4±0.57
II	30	6.16±0.42	6.5±0.42	6.83±0.4	5.5±0.42	6.5±0.5	5.5±0.42
III	200	3±0.36***	5.83±0.79	4.66±0.55*	3.7±0.49*	3.63±0.71**	3.3±0.49*
IV	200	2.16±0.47*	4.33±0.61	3.83±0.47	3.66±0.42**	3.33±0.33**	3.18±0.27**

Values are given as Mean ± SEM for groups of six animals each.

*P<0.05, **P<0.01 and *** P<0.001 as compared to positive control vs extracts, Control rats and drug treated rats.

The study also shows that the extract significantly delayed the reaction time of thermally-induced (hot plate) test. This model is selective for centrally acting analgesics and indicates narcotic involvement [25] with opiod receptors.

CONCLUSION

In conclusion, we can confirm that the aerial methanolic extracts of *P.corymbosa* are endowed with central analgesic properties. However, further study is needed in order to understand the precise mechanism. In future experiments, studies with purified fractions of the extract can be conducted for further pharmacological and toxicological characterization, such as the research of the mechanisms involved in the central and peripheral analgesic effect.

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