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Evaluation of Analgesic Activity of *Berberis Aristata* Dc.-An Experimental Study

KEYWORDS: Analgesic activity, Non-steroidal anti-inflammatory drugs, Berberis aristata.

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ABSTRACT *Pain is an ill-defined unpleasant sensation usually evoked by an external or internal noxious stimulus. The problems associated with the use of non-steroidal anti-inflammatory drugs (NSAIDs) and opioids as analgesics underline the urgent need to screen and identify plant material used as pain relievers in traditional medicine. The purpose of present study was undertaken to assess the analgesic effect of Berberis aristata in*

albino rats and mice. The analgesic action was studied by acetic acid induced writhing, tail flick and hot plate method. In each experiment animals were divided in 5 groups of 6 animals each. 1st group was given normal saline in dose of 5ml/kg, 2nd standard analgesic drug and 3rd, 4th and 5th group Berberis aristata in doses of 50, 100 & 200 mg/kg respectively. Normal saline group serves as a control. In all experiments drugs were given orally.

B. aristata showed significant analgesic activity ($p<0.05$) in all three models used to evaluate analgesic activity as compared to saline treated group.

INTRODUCTION

Pain has been officially defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Pain is the most important symptom which brings the patient to the physician. Analgesics are the drugs that selectively relieve pain by acting on the central nervous system (CNS) or on peripheral pain mechanisms, without significantly altering consciousness.[1] Due to having adverse side effects, like gastric lesions, caused by NSAIDs and tolerance and dependence induced by opiates, the use of these drugs as analgesic agents have not been successful in all the cases. Therefore, analgesic drugs lacking those effects are being searched all over the world as alternatives to NSAIDs and opiates. During this process, the investigation of the efficacy of plant-based drugs used in the traditional medicine have been paid great attention because they are cheap, have little side effects and according to WHO still about 80% of the world population rely mainly on plant based drugs.[2]

Berberis aristata DC. (Berberidaceae) is commonly known as Daruharidra in Bengali, Daruhald & Rasaut in Hindi. In India drug is largely collected in Chamba district of U.P. The chief constituent is berberine, and other reported phytoconstituents are berbamine, armoline, palmatine and oxycanthine.[3]

Berberis aristata DC. is an important medicinal plant used traditionally as an antimicrobial, antibacterial, antipyretic, immunostimulant, laxative, antihemorrhagic, and anti-inflammatory agent.[4] Despite its widespread use in traditional medicine for treatment of various inflammatory disorders, only a few studies have evaluated the efficacy of this medicinal plant.

The present study is aimed for evaluating the analgesic activity of hydroalcoholic extract of Berberis aristata in albino wistar rats and mice.

Materials and Methods

Animals

The study was conducted on healthy albino mice (25-30 gm) and albino wistar rats (100– 150 gm) of either sex, maintained at an ambient temperature of 25 – 35°C with food and water ad

libitum. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) and was executed according to the guidelines of the committee for the purpose of control and supervision of the experiments on animals (CPCSEA), India.

Plant Material

Extraction was done by "maceration" method. First of all 50 gm of the ariel part of plant (leaves and stem) in the dried form were weighted. After that, they were mashed and then added to 1500cc of a solvent (half ethanol and half water) and were shaken by 90 cycle/min for 48 hours until they got homogenous. After that the solutions were filtered with strainer (watmann 0/5mm USA) and put on rotary evaporator to evaporate the solvent. Finally the pure extracts were kept in sterile vials in refrigerator to be used in microbial tests.

In each experiment animals were divided in 5 groups of 6 animals each. 1st group was given

normal saline in dose of 5ml/kg, 2nd standard analgesic drug and 3rd, 4th and 5th group B. aristata in doses of 50, 100 & 200 mg/kg respectively. Normal saline group serves as a

control. In all experiments drugs were given orally.
To study analgesic activity following methods were used:

(1) Acetic acid induced writhing method:
The Acetic acid induced writhing method was assessed on mice. For inducing writhing, animals of each group were challenged with intra peritoneal (i.p.) injection of acetic acid solution in dose of 10 ml/kg of 0.6% in normal saline. Counting of writhing movements were started after 5 minutes of induction through acetic acid and counted over a period of 10 minutes. All the drugs were given once orally and standard analgesic drug used was aspirin in dose of

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100mg/kg.

(2) Tail Flick method:
The tail flick method was assessed on rats using analgesiometer. The instrument has a nichrome wire, which would be heated to the required temperature and maintained by means of heat regulators. The strength of the current passing through the naked nichrome wire was kept constant at 4 Amps. The latency period (reaction time) was noted when the animal responded with a sudden and characteristic flick or tail lifting. A cut-off reaction time was fixed at 10 second to avoid tissue damage. Those rats were included in the study which showed the reaction within the range of 4-6 seconds. The procedure was repeated and reaction time is noted before and after 30 minutes, 60 minutes and 90 minutes. All the drugs were given once orally and standard analgesic drug used was Tramadol in dose of 5mg/kg.

(3) Hot plate method:
The hot plate method was assessed on mice. Animals of each group were challenged with noxious stimuli by placing them into the Perspex cylinder on the heated surface; the temperature of which is maintained at 55.0 ± 0.2° C and a basal latency to a discomfort reaction (licking hind paws or jumping) time was noted. Those mice were included in the study which showed the reaction within 6-8 seconds. A cut-off reaction time was fixed at 15 second to avoid tissue damage. The procedure was repeated and reaction time is noted before and after 30 minutes, 60 minutes and 90 minutes. All the drugs were given once orally and standard analgesic drug used was Tramadol in dose of 5mg/kg.

Statistical Analysis
Results were calculated by one way analysis of variance (ANOVA) followed by Newman-Keuls multiple comparisons. Results were expressed as mean ± SD. P values were calculated referring to the appropriate tables. Values of P<0.05 were considered as statistically significant.

Table- I: Effect of B. aristata **and aspirin on acetic acid induced writhing movement in albino mice (n=6)**

Drug	Dose (mg/kg, oral)	Number of writhing movement ± SD	% inhibition in writhing-Movement
Saline	5 ml	17.67 ± 1.53	
Aspirin	100	2.33 ± 0.57*	86.82
B. aristata	50	6.33 ± 0.56*	64.18
B. aristata	100	3.67 ± 0.57*	79.24
B. aristata	200	2.66 ± 0.57*	84.95

*P < 0.05 (as compared to saline treated group)

Table- II: Effect of B. aristata **and tramadol on algesia induced by tail flick method in albino rats (n=6)**

Drug	Dose(mg/kg, oral)	Reaction time(seconds)±SD			
		Before treatment	After treatment		
			30 min	60 min	90 min
Saline	5 ml	3.03±0.09	3.12±0.19	3.01±0.11	3.21±0.08
Tramadol	5	3.55±0.14	4.56±0.16*	5.12±0.24*	6.85±0.19*
B. aristata	50	4.0±0.13	3.32±0.27*	4.13±0.11*	4.86±0.23*
B. aristata	100	3.14±0.07	3.84±0.18*	4.71±0.19*	5.12±0.12*
B. aristata	200	3.80±0.12	4.17±0.21*	4.75±0.28*	5.91±0.15*

*P<0.05 (as compared to saline treated group)

Table – III: Effect of B. aristata **and tramadol on algesia induced by hot plate method in albino mice. (n=6)**

Drug	Dose(mg/kg, oral)	Reaction time(seconds)±SD			
		Before treatment	After treatment		
			30 min	60 min	90 min
Saline	5 ml	5.90±0.20	5.85±0.25	5.88±0.25	5.81±0.31
Tramadol	5	5.90±0.40	8.89±0.25*	11.22±0.36*	14.15±0.84*
B. aristata	50	5.81±0.24	5.92±0.31*	7.96±0.32*	8.78±0.41*
B. aristata	100	5.78±0.32	6.51±0.22*	8.11±0.22*	10.23±0.45*
B. aristata	200	5.71±0.22	8.05±0.62*	9.87±0.44*	12.14±0.63*

*P<0.05 (as compared to saline treated group)

RESULTS:
(i) Acetic acid induced writhing: (Table I)
The analgesic activity was expressed as percent reduction in mean number of writhing movement comparing with control as 100% writhing movement. Writhing response is suppressed significantly (p<0.05) by standard drug as well as by B. aristata at the dose of 50, 100, 200 mg/kg. At the dose of 50 mg/kg B. aristata showed 64.18 % reduction in acetic acid induced writhing response, while at dose of 100 mg/kg and 200 mg/kg % reduction is 79.24% and 84.95% respectively. Standard drug Aspirin showed 86.82% suppression. B. aristata was found to increase the basal reaction time in a dose dependent manner.

ii) Tail flick method: (Table II)
In this method latency period (reaction time) was noted when the animal responded with a sudden and characteristic flick. In the present study, B. aristata showed a significant (p<0.05) analgesic effect compared to that of control group at all the three doses (50, 100, 200 mg/kg) used.

(iii) Hot plate method: (Table III)
The analgesic activity was expressed as percent elevation in mean reaction time in B. aristata treated group taking control as 100% reaction time. B. aristata was found to increase the basal reaction time in a dose-dependent manner. B. aristata at the dose of 50, 100, 200 mg/kg showed statistically significant analgesic activity (p<0.05) compared to saline treated group.

DISCUSSION:
Pain sensation are received at different levels like peripheral, spinal and at supra spinal level. In our study, three of the most common phasic nociceptive tests have been investigated: writhing response, tail-flick, hot-plate method. Writhing response of the animals to an intra-peritoneal injection of noxious chemical such as acetic acid and thermal stimuli in tail flick and hotplate method were used to screen both peripheral and central analgesic activity, respectively. The results of the present study show significant anti nociceptive effect of B. aristata in writhing response (Table I) tail flick method (Table II) and in hot plate method (Table III) at all three doses used (50, 100, 200 mg/kg).

Acetic acid induced writhing is used to evaluate drugs acting on pain produced by inflammation and local irritation which involves release of mediators of inflammation like

prostaglandins, histamine, serotonin, substance P etc. Inhibition of cyclo-oxygenase in the peripheral tissues, results in interference with the mechanism of transduction in pri-

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mary afferent nociceptors because it is principal enzyme responsible for production of inflammatory mediators.[8] Cyclo-oxygenase enzyme inhibiting activity of B. aristata may be responsible for inhibition of peripheral pain mechanism.[6]

Tail Flick method is predominantly a spinal response and Hot Plate method is predominantly supraspinal response.[7] The mechanism responsible for the central analgesic activity of B. aristata is probably mediated via opioid receptors.

Conclusion:

Our study provide evidence for analgesic activity of Berberis aristata DC. However, further investigation is required to isolate the active constituents responsible for this activity and to elucidate the exact mechanisms of action.

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