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A STUDY ON THE ANALGESIC AND ANTI-INFLAMMATORY ACTIVITY OF *SCUTELLARIA DISCOLOR* COLEBR IN EXPERIMENTAL ANIMALS

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ABSTRACT: The genus *Scutellaria* has many species. But only a few species are investigated for the treatment of many ailments. Despite the extensive use of traditional medicine against several diseases, scientific studies of Scutellaria discolor are less. The present study is taken up to investigate the analgesic and anti-inflammatory actions of the acetone extract of *S. discolour* (SDA)using tail flick method with Analgesiometer and carrageenan induced hind paw edema model respectively using albino rats. The study of acute toxicity of the extract is done so as to determine the dose of the extract and to save the experimental animals. Pethidine and aspirin were used as the standard drugs for the analgesic and anti-inflammatory experiment, respectively. In tail-flick test, SDA induced a significant increase ($p<0.05$, $p<0.001$) in the reaction time to pain stimulation compared to the control showing its analgesic activity which was comparable to that of pethidine. In carrageenan-induced paw edema test, SDA showed significantly lower ($p< 0.001$) mean paw volume compared to the control group. But percentage inhibition of edema was greater in the aspirin group when compared to SDA. The results show that *S. discolor* analgesic and anti-inflammatory activity supporting the reports of its uses in traditional medicine against inflammation and pain.

INTRODUCTION: This genus *Scutellaria*, commonly known as skullcaps [1] includes about 350 species that are widespread in biodiversity hotspots of East Asia, the United States, and Europe [2]. This genus has received considerable attention in recent years due to its confirmed pharmacological effects, isolation of potential drug leads, and study of only 35 out of the reported 350 species [3, 4].

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A particular species, *Scutellaria discolor* Colebr. belonging to this genus, is an important medicinal plant that is used as a source of antipyretic, antidote and anti-inflammatory agents for the treatment of colds, gastroenteritis, tympanitis, and other diseases in China and Nepal [4, 5].

This species is widely distributed in the Indo-Burma biodiversity hotspot and used as traditional medicine in Manipur, India, to treat various clinical conditions associated with fever and in conditions like piles, sprains, cramp, aching, twitching of muscles, and swellings [6, 7]. Therefore, it is assumed that the plant may have anti-inflammatory and analgesic action. The objective of this study was to investigate the analgesic and anti-inflammatory

actions of *Scutellaria discolour* in the experimental animals.

MATERIALS AND METHODS:

Drugs and Chemicals: Aspirin (Bayer AG, Germany), pethidine (Neon Labs) and carrageenan (Hi-Media Laboratories Pvt. Ltd., Mumbai) were purchased from the respective companies. All other chemicals and solvents used were of analytical grade.

Plant Material: The whole plant was collected from the hilly area of Chandel, Manipur, India, and identified as *S. discolor* by Plant Systematics and Conservation Laboratory, Plant Bioresources Division, Institute of Bioresources and Sustainable Development (IBSD), Manipur, India. A voucher specimen (IBSD/M-194) was deposited to the IBSD herbarium.

Preparation of *S. discolor* Acetone (SDA) Extract: The whole plant was air-dried, pulverized and 500gm of the plant was exhaustively extracted by soaking in acetone. The filtrate was then dried using a vacuum rotary evaporator and lyophilized with the help of Thermo Modulyod, Waltham, MA, USA, to yield 91gm of acetone extract of *Scutellaria discolor* (SDA).

Animals: Healthy male albino rats weighing 150-200gm were used for the experiment. They were fed with a standard laboratory diet and water *ad libitum* with due care to prevent coprophagy. All animals were kept in polypropylene cages and acclimatized in the laboratory for at least one week before the experiment. All the experimental procedures were followed as per the guidelines of the Institutional Animals Ethics Committee (IEAC), RIMS, Imphal, and the IAEC approval number is 1596/GO/a/12/CPCSEA. All drugs were suspended in 2% gum acacia and were administered in a volume of 5 ml/kg body weight.

For the tail-flick model, albino rats were divided into five groups of six animals, each as follows:

Groups	Treatments
Group A	Control (2% gum acacia, po)
Group B	SDA1 (50mg/kg, po)
Group C	SDA2 (100mg/kg, po)
Group D	SDA3 (200mg/kg,po)
Group E	Standard (Pethidine, 5 mg/kg, ip)

For the carrageenan-induced paw edema model, albino rats were divided into three groups of six animals each as follows:

Groups	Treatments
Group I	Control (2% gum acacia, po)
Group II	SDA (150mg /kg, po)
Group III	Standard (Aspirin, 100mg/kg, po)

Toxicity test: Acute oral toxicity study for the extract was carried out using OECD/ OCED Guideline [8]. Only 6 healthy rats were recruited and the extract was administered orally as per body weight up to a maximum of 2000mg /kg. The rats were kept under observation for a period of 14 days.

Tail Flick Method: The analgesic action of SDA was measured using a tail-flick method of Amour and Smith [9] with some modification. Reaction time in seconds was used as the unit for measurement of pain and an increase in reaction time was indicative of analgesia. The current intensity passing through the naked nichrome wire was maintained at 6 amperes. The distance between the heat source and the tail skin was 1.5 cm, and the site of application of the radiant heat to the tail was maintained at 2.5cm from the root of the tail. The time taken by rats to withdraw (flicking response) the tail from the hot wire was recorded as the reaction time. The reaction time of the normal rat was taken as 3-4 sec. The cut-off reaction time was fixed at 10sec so as to avoid any tissue damage. In all the groups, the reaction time was recorded prior (0 min) to drug administration and at 30, 60 and 120 minutes after drug administration

Carrageenan Induced Paw Edema Model: The anti-inflammatory effect of SDA was measured using the method described by Winter *et al.*,[10]. Edema was induced by sub plantar injection of 100 uL of freshly prepared carrageenin (1% in normal saline solution) into the right hind paws of each rat 1 h after the drug administrations. The paw was marked with ink at the level of the lateral malleolus and immersed in mercury up to this mark. The paw volume was measured plethysmographically immediately after injection *i.e*., 0 and 1, 2, 3, 4 and 5 h after the carrageenan injection. An increase in paw thickness was measured as the difference in paw thickness at 0 hr and paw thickness at the respective hrs of observations.

The percentage of inhibition of paw edema was calculated using the following formula.

Percentage inhibition = Ct-C0) control - (Ct-C0) treated / (Ct-C0) control × 100

Where Ct is the paw size at t hour (t = 1, 2,…n) after carrageenan injection and C0 is the paw size before carrageenan injection.

Statistical Analysis: Results are expressed as mean ± Standard deviation (SD). Data were analyzed using Graph pad Instat 3 software.

Comparison between different groups was done by One-Way Analysis of Variance (ANOVA) followed by Tukey- Kramer multiple comparisons test.

P-value less than 0.05 was considered statistically significant.

RESULTS:

Acute Toxicity test: The acetone extract of *Scutellaria discolor* (SDA) was found to be safe in the doses tested. There was no mortality seen up to a dose of 2000mg/kg body weight. p.o.

Tail Flick Method: The reaction times in seconds of all the groups recorded before drug treatment and 30, 60, and 120 mins after drug treatment are shown in **Table 1**. Compared to the control group, SDA showed a significant increase (*p<0.05, ***p<0.001) in reaction time in all the tested concentrations. It was observed that the increase in reaction time was more significant after 60 minutes. At higher doses, *i.e.*, 100 and 200mg/kg, SDA showed nearly similar activity to that of the standard drug, Pethidine. The onset of analgesic action was not quick, took time, but the duration of analgesic action was maintained for a longer time.

TABLE 1: EFFECT OF *SCUTELLARIA DISCOLOR* ON THE REACTION TIME AT VARIOUS TIME INTERVALS ON TAIL-FLICK METHOD IN RATS

Group	Reaction time (in seconds) before drug treatment (Mean ± SD)	Reaction time (in seconds) after drug treatment (Mean ± SD)		
		30 min	60 min	120 min
Control	4.16±0.75	4.33±0.82[a]	4.66±0.52[a]	4.92±0.51[a]
SDA 1	4.33±0.52	5.33±0.52[b]*	6.33±0.52[b] ***	6.5±0.55[b] ***
SDA 2	4.16±0.75	6.33±0.51[c]***	7.16±0.41[bc] ***	7.66±0.52***
SDA 3	4.5±0.55	6.16±0.41[c] ***	7±0.63[bc] ***	7.66±0.52***
Standard	4.67±0.51	6.67±0.51[c] ***	7.5±0.55[c] ***	8.17±0.75***
p value	0.5656	<0.0001	<0.0001	<0.0001

Mean ± SD (n=6). Within a column, means marked with different superscript letters are significantly different. *p<0.05, **p<0.01,***p<0.001 when compared with the corresponding values of control.

Carrageenan Induced Paw Edema Model: The effect of SDA on edema is presented in **Table 2** and **Fig. 1.** The basal mean paw volume was comparable in all the groups (p = 0.5964). Carrageenan injection into the hind paw induced a progressive increase in edema.

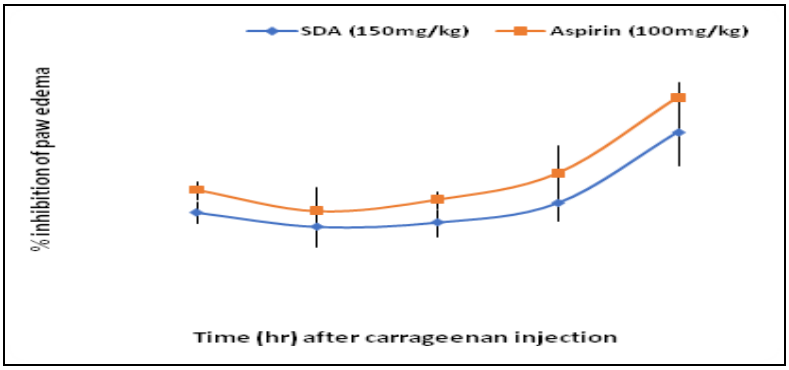

FIG. 1: PERCENTAGE INHIBITION OF CARRAGEENAN INDUCED PAW EDEMA BY *SCUTELLARIA DISCOLORAT* VARIOUS TIME INTERVALS

However, the mean paw volume of the SDA treated group was significantly lower when compared to the control group (p< 0.001) with 30, 39, and 73% inhibition of paw edema at 3rd, 4th, and 5th hour. Percentage inhibition was greater in the aspirin group when compared to SDA.

TABLE 2: EFFECT OF SCUTELLARIADISCOLOR IN CARRAGEENAN INDUCED PAW EDEMA IN RATS

	Initial Paw Volume (ml)	Paw volume (ml) after carrageenan injection(Mean ± SD)				
Group	0 hr	1hr	2hr	3hr	4hr	5hr
I (Control)	0.98±0.04	1.38±0.02	1.5±0.07	1.49±0.05	1.4±0.07	1.32±0.04
II (SDA)	0.95±0.08	1.21±0.02*	1.34±0.06$^{\alpha}$	1.31±0.04*	1.19±0.04*	1.04±0.05*
III (Aspirin)	0.98±0.04	1.19±0.01$^{\beta\#}$	1.3±0.05$^{\beta\#}$	1.29±0.02$^{\beta\#}$	1.17±0.05 $^{\beta\#}$	1.01±0.02$^{\beta\#}$
p value	0.5964	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Tukey-Kramer Multiple Comparisons Test: α - p<0.01, when Group I vs Group II, * - p<0.001, when Group I vs Group II, β – p<0.001, when Group I vs Group III, # - p>0.05, when Group II vs Group III

DISCUSSION: Many species belonging to the genus *Scutellaria* have been reported for their anti-inflammatory activity. *Scutellaria baicalensis*, *Scutellaria barbata*, and *Scutellaria galericulata* were investigated for the analgesic and anti-inflammatory action by many researchers like Bahram H *et al.* [11], Hsin-Lan Liu *et al.* [12] and Kai Xiao [13] and for the use of anti-arthritic and anti-inflammatory action by Yimam *et al.* ***[13]***. In this study, for the first time, the analgesic and anti-inflammatory effect of the acetone extract of *Scutellaria discolor* was investigated using the tail flick method and carrageenan-induced paw edema method, respectively.

The analgesic effect of *Scutellaria discolor* is almost tallied with the findings of the above-mentioned studies. However, the onsets of analgesic action of the SDA extract is not quick or the onset of anti-inflammatory action is slow and may commence both actions after 30 min and last up to 120 min. The present result of the administration of SDA extract may be due to the suppression of thermal stimulation-induced nociception pain. It is now demonstrated that *Scutellaria discolor* has analgesic and anti-inflammatory activities and could be the reason for its wide use in traditional medicine to treat different types of pain.

CONCLUSION: The *Scutellaria discolour* acetone extract has analgesic and anti-inflammatory activities in albino rats, supporting traditional healers' claims of the use of the plants as analgesics and anti-inflammatory. Further, it is suggested to undertake a detailed study of the plant extract by using good, precise, accurate, sensitive tools, equipment and methods, etc., to find out its mechanism of action and the active compounds responsible for the effects.

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