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Central and Peripheral Analgesic Activity of Turmeric Rhizome Collected from Uttarakhand, India

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The thermal stimuli in hotplate test and the writhing response of the animals to an intra-peritoneal injection of noxious chemicals were used to screen both centrally and peripherally acting analgesic activity. The methanolic extract of *Curcuma longa* was investigated for its antinociceptive activity in animal models collected from Ukhimath and Haldwani, in dose dependent manner. Ibuprofen and indomethacin, were used as standard drugs for different activities and saline water was used as control. The analgesic action of *Curcuma longa* can be attributed to reduce the peripheral nociception by inhibition of prostaglandin release. The result from present study indicates that the methanolic extract of *Curcuma longa* rhizome collected from Ukhimath (SP-1) showed significant ($p < 0.05$) peripheral analgesic activity with 42.25 % inhibition at dose level of 100 mg/kg body weight concentration, which was close to the effect induced by standard drug ibuprofen causing 43.91 % inhibition. Methanolic extract of Ukhimath collection at the dose level of 50 and 100 mg/kg body wt., manifested significant central analgesic activity (3.33 ± 0.02 to 4.16 ± 0.02 and 3.37 ± 0.02 to 4.19 ± 0.02, respectively) which continued until 120 min after administration; whereas the extract of Haldwani collection at the dose of 50 and 100 mg/kg body wt., showed intense effects just like the reference drug indomethacin at 60 min which continued till 120 min, (3.24 ± 0.03 to 4.08 ± 0.03 and 3.30 ± 0.02 to 4.10 ± 0.04, respectively). In our study a wide variation are observed in different samples within the activities, which might be because of climatic, edaphic and genetic variation.

Keywords: Antinociceptive, Hot plate method, Acetic acid writhing test, Turmeric.

INTRODUCTION

The use of medicinal plants for the treatment of many diseases is associated to folk medicine from different parts of the world. Natural products from some plants, fungi, bacteria and other organisms continue to be used in pharmaceutical preparations either as pure compounds or as extracts. There is a great variety of compounds that can be extracted and characterized from plants. One good example is the curcumin, a polyphenolic compound found in *Curcuma longa*, commonly known turmeric. Turmeric is one of the most important medicinal plants which extensively used in Ayurveda, Unani and Siddha medicine as home remedy for various diseases. It is used in the form of powder as a common colouring spice and also known to have some nourishing properties. It is one of the essential components of great Indian curry powder. In medieval Europe, turmeric became known as Indian saffron, since it was widely used as an alternative to the far more expensive saffron spice.

The rhizome is pungent, bitter, heating. The curcuma is laxative, anthelmintic, vulnerary, tonic, alexiteric, emollient and improves the complexion. It is beneficial for diseases of blood, leucoderma, scabies, inflammations, ozoena, bad taste in the mouth, biliousness, dyspepsia, elephantiasis, snake bite, small pox, boils, bruises, sprains, *etc*. as discussed in Ayurveda. Turmeric is a yellow/brown powder and it has a slight earthy flavour and little aroma. It is known for its colour and for its health-giving properties.3-5 % yellow pigments that are not volatile in steam (curcuminoids), consisting of cucurmin 50-60 %, monodesmethoxycurcumin and bisdeesmethoxycurcumin. 2-7 % essential oil, comprising mainly bisabolane, guaiane and germacranesesquiterpenes: turmerone, arturmerone, zingiberene, curlone, *etc*. The high content of bisabolane derivatives distinguishes turmeric from other curcuma species.

Current research has focused on turmeric's antioxidant, hepatoprotective, anti-inflammatory, anticarcinogenic and antimicrobial properties in addition to its use in gastric ulcer, cardiovascular disease and gastrointestinal disorders and wound healing [1]. The aim of this study is to investigate *in vivo* antinociceptive activity of methanolic extract of turmeric rhizome and the effect of climate and altitude on it.

EXPERIMENTAL

The rhizomes of turmeric was collected from two different regions, one from higher altitude place Ukhimath, district Rudraprayag and another one from plain region place Haldwani,

district Nanital. All the samples were washed thoroughly under tape water, sliced, air dried, ground to fine powdered and dipped in methanol.

Animals: Total 6 groups of 6 mice in each group were selected to evaluate the antinociceptive activities of extracts of *Curcuma longa* (L.). The experiments were carried out with two concentrations of extracts (50 and 100 mg/kg body wt.). Ibuprofen and indomethacin were used as standard drugs for different activities and saline water used as control and administered orally to mice in the experiment.

Peripheral analgesic activity (Writhing effect): Glacial acetic acid was administered intraperitoneally to the experimental animals to create pain sensation. As a result, the animals squirmed their bodies at regular intervals out of pain. This squirm or contraction of the body is termed as writhing. Any substance that has got analgesic activity is supposed to reduce the number of writhing of animals within a given time and with respect to the control group [2]. At zero hour 0.2 mL of extracts (50 and 100 mg/kg), standard drug (ibuprofren-40 mg/kg body wt.) and control (saline water) were administered orally. After 40 min, glacial acetic acid (1 % at dose of 0.1 mL/10 g body weight) was administered intraperitoneally to each mice of the acetic acid, the number of writhing were counted for 1 min for each mouse. The inhibition of writhing in mice by the oleoresins was compared against inhibition of writhing by the standard analgesic ibuprofen. Percentage of pain protection was calculated as per following formula:

$$\text{Writhing (\%)} = \frac{T}{C} \times 100 \; ; \; \text{Inhibition (\%)} = \frac{C - T}{C} \times 100$$

where, T = treatments (group II-X); C = control saline group (I).

Central analgesic activity (Hot plate method): The hot-plate test was performed to measure analgesic response latencies [3]. It is a simple and sensitive method for studying analgesic and hyperanalgesic reaction in mice. The hot-plate was maintained at 55 ± 0.5 °C and the mice were placed into Perspex cylinder on the heated surface and the time (s) to discomfort reaction (licking paws or jumping) was recorded as response latency, prior to and 30, 60, 120 and 150 min after administration of the extracts at the dose rate of 50 and 100 mg/kg body wt., orally. As positive control, standard drug indomethacin (5 mg/kg body wt.) and for negative saline water (0.2 mL) given orally were used. A latency period of 20 s was defined as complete analgesia and the measurement was terminated if it exceeded the latency period in order to avoid injury.

Statistical analysis: Data were expressed as the mean ± SEM. The data were analyzed using one way analysis of variance (ANOVA) followed by Dunett's test. Data were considered different at significance level of $p < 0.05$. The test has been done using SPSS version 16.0.

RESULTS AND DISCUSSION

The antinociceptive effect of extracts and standard were assessed using Writhing effects in mice and results have been illustrated in Table-1. Extracts exhibited significant antinociceptive activity in a dose dependent manner. Methanolic extract of *Curcuma longa* rhizome collected from Ukhimath (SP-1) showed significant ($p < 0.05$) analgesic activity with 42.25 % inhibition at dose level of 100 mg/kg body weight concentration, which was close to the effect induced by standard drug ibuprofen causing 43.91 % inhibition. The Haldwani collection (SP-2) showed an inhibition of 36.02 % at a dose of 100 mg/kg body wt. SP-1 at the dose of 50 mg/kg body weight showed 34.4 % inhibition followed by Haldwani (23.09 %) (SP2). The result showed that the mean difference was significant at the level of $p < 0.05$ for both the extracts and standard as compared to control.

The acetic acid induced writhing test was carried out to confirm the peripheral analgesic activity of extract. The acetic acid used in this test increased the prostaglandin level (mainly PGE_2) in the peritoneal fluid of the mice. Prostaglandins induce abnormal constriction by activating and sensitizing the peripheral chemo-sensitive nociceptors which are mostly responsible for causing inflammatory pain. In our study, methanolic extracts of *Curcuma longa* collected from different places, significantly attenuated the writhing in mice in response to acetic acid administration, although to a slightly lesser extent compared to the highly potent ibuprofen. Hence, the analgesic action of turmeric extract can be attributed to reduce the peripheral nociception by inhibition of prostaglandin release. Recently writhing effect of hydrazinocurcumin was reported on mice [4].

Hot plate reaction time in indomethacin treated mice was maximum at 60 min while different extracts of *Curcuma longa* exhibited their effects by increasing the paw licking and jumping time on hot plate in dose dependent manner. Methanolic extract of SP-1 at 50 and 100 mg/kg body wt., concentration manifested the significant analgesic activity (3.33 ± 0.02 to 4.16 ± 0.02 and 3.37 ± 0.02 to 4.19 ± 0.02, respectively) which continued until 120 min after administration; whereas SP-2 methanolic extract at the dose of 50 and 100 mg/kg body wt., concentration showed intense effects just like the reference

TABLE-1
ANTI-NOCICEPTIVE ACTIVITY OF EXTRACTS OF *Curcuma longa* COLLECTED FROM UKHIMATH (SP-1) AND HALDWANI (SP-2) (WRITHING EFFECT) (Mean ± SE, n = 6)

Group	Treatment	Dose (mg/kg)	Number of Writhings	Writhings (%)	Inhibition (%)
1	Control	0.2 mL	156	100	–
2	Ibuprofen	40	87.4[b]	56.03	43.91
3	SP-1 50	50	102.33[ab]	65.60	34.40
4	SP-1 50	100	90.06[a]	57.73	**42.25**
5	SP-2 100	50	119.5[ab]	76.60	23.29
6	SP-2 100	100	99.83[ab]	64.00	**36.02**

One way ANOVA followed by Dunetts multiple comparison test
[a]Significant ($P < 0.05$) as compared to control; [b]Significant ($P < 0.05$) as compared to drug

TABLE-2
ANTI-NOCICEPTIVE ACTIVITY OF METHANOLIC EXTRACTS OF *Curcuma longa* COLLECTED FROM UKHIMATH (SP-1) AND HALDWANI (SP-2) (HOT PLATE METHOD) (Mean ± SE, n = 6)

Groups	Treatments	Dose (mg/kg)	Hot plate reaction time (min)					
			0	30	60	90	120	150
1	Control	0.02 mL	3.05 ± 0.03	3.01 ± 0.02	3 ± 0.04	2.94 ± 0.03	2.9 ± 0.05	2.88 ± 0.02
2	Indomethacin	5	3.36 ± 0.03[a]	3.82 ± 0.03[a]	4.46 ± 0.03	4.31 ± 0.05[a]	4.11 ± 0.03[a]	3.92 ± 0.02[a]
3	SP-1	50	3.33 ± 0.04[a]	3.80 ± 0.02[a]	4.52 ± 0.02[a]	4.33 ± 0.03[a]	4.16 ± 0.02[b]	4.02 ± 0.03
4	SP-1	100	3.37 ± 0.02[a]	3.86 ± 0.03[a]	4.71 ± 0.02[ab]	4.37 ± 0.03[a]	4.19 ± 0.02[ab]	4.08 ± 0.04[ab]
5	SP-2	50	3.24 ± 0.03[ab]	3.79 ± 0.04[a]	4.45 ± 0.03[ab]	4.14 ± 0.02[a]	4.08 ± 0.03[ab]	3.89 ± 0.03[a]
6	SP-2	100	3.30 ± 0.02[ab]	3.81 ± 0.02[a]	4.5 ± 0.03[a]	4.2 ± 0.03[a]	4.10 ± 0.04[ab]	3.91 ± 0.03[a]

One way ANOVA followed by dunetts multiple comparison test
[a]Significant ($P < 0.05$) as compared to control; [b]Significant ($P < 0.05$) as compared to drug

drug indomethacin at 60 min which continued till 120 min, (3.24 ± 0.03 to 4.08 ± 0.03 and 3.30 ± 0.02 to 4.10 ± 0.04, respectively) (Table-2). On the bases of Dunetts test SP-1 showed that the mean difference was not significant as compared to standard at the level $p < 0.05$, this reveals that its activity is much more similar to indomethacin.

The hot plate test measures the complex responses to a non-inflammatory, acute nociceptive input and is one of the models normally used for studying central nociceptive activity [5]. Antagent that causes the prolongation of the hot plate lantency using this test must be centrally acting [6]. Therefore, the methanolic extracts of *Curcuma longa* collected from Ukimath and Haldwani might have a central activity which is reveled by the efficacy against thermal stimulus.

Result shows that this plant is a good natural source for antinociceptive activity. In this study a wide variation are observed in different samples within the activities, which might be because of climatic, edaphic and genetic variation. As this plant easily available and the methanolic extract is showing better activity suggesting that this plant is a cost effective natural treatment product. As the cost of the treatment rising, developing a cost effective remedies will definitely gives a better option and opportunities to treat chronic diseases.

Conclusion

The analgesic action of *Curcuma longa* can be attributed to reduce the peripheral nociception by inhibition of prostaglandin release. The result from present study indicates that the methanolic extract of *Curcuma longa* rhizome collected from Ukhimath (SP-1) showed significant ($p < 0.05$) peripheral analgesic activity with 42.25 % inhibition at dose level of 100 mg/kg body weight concentration, which was close to the effect induced by standard drug ibuprofen causing 43.91 % inhibition. Methanolic extract of Ukhimath collection at the dose level of 50 and 100 mg/kg body wt., manifested significant central analgesic activity (3.33 ± 0.02 to 4.16 ± 0.02 and 3.37 ± 0.02 to 4.19 ± 0.02, respectively) which continued until 120 min after administration. Result shows that this plant is a good natural source for antinociceptive activity. In our study a wide variation are observed in different samples within the activities, which might be because of climatic, edaphic and genetic variation.

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