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Analgesic property of different extracts of *Curcuma longa* (Linn.): An experimental study in animals

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Abstract

Different extracts of *Curcuma longa*, code named as PC/CL/SWP05, CL/111107506 and PT/0606188, each at three doses 100, 200 and 400 mg/kg were evaluated for their analgesic activity using different animal models of analgesia. PT/0606188 exhibited significant analgesic activity in the tail flick test at 400 mg/kg one hour after administration. CL/111107506 exhibited significant analgesic activity in the tail withdrawal test, one hour after administration at a dose of 100 mg/kg. All the three extracts significantly reduced the number of writhes in the acetic acid test except for PT/0606188 at a dose of 100 mg/kg. PC/CL/SWP05 demonstrated only peripheral analgesic activity while CL/111107506 and PT/0606188 demonstrated both central and peripheral analgesic activities.

Key Words: *Curcuma longa*, Analgesic activity, mice.

1. Introduction

Curcuma longa Linn. commonly known as turmeric, belongs to the family Zingiberaceae. Its rhizome is widely used in indigenous medicine and as household remedies [1]. It is also applied in poultices to relieve pain and inflammation [2]. Curcuma is also being used in traditional Chinese medicine as a pain relieving plaster along with other herbs [3].

The herb contains curcumin as the active ingredient, which is a yellow coloured phenolic pigment obtained from the powdered rhizome of *C. longa* Linn. In the crude extracts of *C. longa* about 70 to 76 % curcumin is present, along with about 16% demethoxycurcumin and 8% bisdemethoxycurcumin [4].

Studies have demonstrated a wide spectrum of therapeutic effects, such as anti-inflammatory [5-7], antioxidant [8], antitumor [9, 10], antibacterial [11], antifungal [12], antiviral [13],

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anti-spasmodic [14], immunomodulation [15] and hepatoprotective [16] activities. Recently its potential utility in acquired immune deficiency syndrome (AIDS) was demonstrated [17].

A few studies have shown that chronic administration of curcumin produces analgesic effect in different animal models of analgesia [18, 19]. Curcumin also suppresses neuropathic pain induced by chronic sciatic nerve ligation [20]. But there is no evidence of analgesic effect caused by acute administration of curcumin, and hence the need for this study.

2. Materials and methods

2.1 Experimental animals

Adult Wistar rats (180-250g) and Swiss Albino mice (15-45g) of either sex were used for the experiments. The animals were housed in polypropylene cages (3 per cage) at a temperature of 28+/-5 degree Celsius and 12 h light/dark cycle. Animals were fed with Hindustan Lever chow pellets and water ad libitum. Ethical approval was obtained prior to experimentation.

2.2 Drugs

CL/111107506 was a commercially available purified extract fraction derived from the rhizomes of *Curcuma longa*. The fraction was standardized to contain >95% w/w of total curcuminoids (comprising of curcumin, demethoxycucrcumin and bisdemethoxy-cucrcumin). The extract fraction left after the purification of CL/111107506 was distilled under high vacuum to get PT/0606188 as yellow oil. The marc (remaining rhizomes) left after the extraction of CL/111107506 was further extracted with water by refluxing (herb to solvent ratio 1:3, three extraction washes, each for two hours). The combined liquid extract was concentrated under vacuum at less than 75 degree Celsius and spray dried to get PC/CL/SWP05.

Carboxymethylcellulose (CMC) was used as the control. The positive controls were pentazocine for tail flick and tail immersion tests, and diclofenac for acetic acid writhing test.

2.3 Experimental design

2.3.1 Experimental groups

Two different sets of rats were randomized into 11 different groups (n=6) for tail flick test and tail immersion test respectively. Mice were randomized into 11 different groups (n=6) for acetic acid writhing test. The groups were: Group 1 served as vehicle control and received Carboxymethylcellulose (CMC) 1 % solution and Group 2 served as positive control and received either Pentazocine (for tail flick and tail immersion tests) or Diclofenac sodium (for acetic acid writhing tests). Diclofenac sodium was used at 10 mg/kg p.o. and Pentazocine was used at 10 mg/kg intraperitoneally. Groups 3, 4 and 5 were administered PC/CL/SWP05 at doses of 100, 200 and 400 mg/kg respectively. Groups 6, 7 and 8 were administered CL/111107506 (100, 200 and 400 mg/kg respectively) and Groups 9, 10 and 11, PT/0606188 at 100, 200 and 400 mg/kg respectively.

2.3.2 Experimental methods

2.3.2.1 Tail Flick Test in rats [21]

The tail received radiant heat from a wire heated by passing a current of 6 mA. The time taken for the withdrawal of the tail was recorded as tail flick latencies in seconds. The withdrawal response was recorded before, 1 h and 2 h after the administration of the compounds. The cut-off time for determination of latent period was taken as 40 sec [22] to avoid injury to the skin and based on our pilot studies. Pentazocine was used as positive control.

2.3.2.2 Tail Immersion Test in rats [23]

The distal 5 cm of the tail was immersed in water maintained at about 55 deg. Celsius. The

time taken for the withdrawal response was recorded before, 1 h and 2 h after administration the compounds. The cut-off time was fixed at 15 sec to prevent injury to the tail. Pentazocine was used as positive control.

2.3.2.3 Acetic acid induced writhing response in mice [24]

Acetic Acid 0.6% was administered at a dose of 10 mg/kg. The test drugs were administered 1 hr before administering acetic acid. The number of writhes was recorded 10 min after administering acetic acid for the next 10 min. Diclofenac sodium was used as positive control.

2.4 Statistical analysis

The statistical analysis was done using SPSS (Version 7.0) software, which is commercially available. The values are expressed as Mean +/ - S.D. Statistical significance was calculated using the one-way ANOVA followed by the post-hoc Tukey Honestly Significant Difference test. p= 0.05 was considered to be significant.

Table 1. Analgesic activity of mice (n=6 per group) in the tail flick, tail withdrawal and acetic acid writhing test at baseline, 1 h and 2 h after administration of different drugs.

Name	Tail Flick Latencies (sec)			Tail Withdrawal latencies (sec)			Acetic Acid test (no.)
	Base Line	1h	2h	Base Line	1h	2h	No. Writhes
Vehicle	3.85±0.93	3.80±1.05	3.52±1.06	1.34±0.32	1.59±0.43	1.60±0.44	45.17±5.67
Positive Control	5.33±1.99	9.71±4.96*	10.35±2.43*	2.55±0.93	3.55±0.56*	4.36±1.09*	29.11±6.57*
PC/CL/ SWP05 100	4.33±1.64	5.32±2.54	5.68±3.03	1.64±0.46	2.32±0.53	3.15±2.13	26.67±5.65*
PC/CL/ SWP05 200	3.53±0.68	5.30±1.91	4.35±1.99	1.89±0.58	2.77±0.82	2.45±0.79	33.17±9.72*
PC/CL/ SWP05 400	4.02±0.97	5.84±2.71	4.50±1.89	2.65±1.64	2.85±1.52	2.72±1.36	26.67±8.45*
CL/111107506 100	4.00±0.97	3.92±1.39	4.67±2.93	1.94±0.33	3.38±0.71*	3.00±0.37	24.00±4.56*
CL/111107506 200	3.97±0.97	3.22±1.80	3.07±1.22	1.56±0.39	2.67±1.24	2.38±0.48	29.33±1.21*
CL/111107506 400	4.11±0.97	3.08±0.85	3.24±1.16	1.70±0.37	2.84±0.58	2.67±0.75	24.17±3.66*
PT/0606188 100	5.22±1.17	8.16±2.96	6.33±0.77	2.84±2.00	2.73±1.09	2.78±0.65	41.83±5.38
PT/0606188 200	5.37±1.39	6.83±2.50	6.16±0.65	2.41±0.49	2.71±0.49	2.54±0.58	32.17±4.67*
PT/0606188 400	4.22±1.42	9.74±3.11*	5.41±0.72	2.25±0.73	2.72±0.78	2.36±0.55	27.67±6.86*
F (df 10, 58)	1.641	5.205	9.384	1.824	2.423	3.653	7.665
Significance	0.118	0.000	0.000	0.076	0.017	0.001	0.000

* Significantly different from vehicle control.

3. Results

The results are presented in Table (1).

Tail flick latencies of different groups did not differ significantly at baseline. (P= 0.118). The latencies of different groups differed significantly from each other at 1 hour (P= 0.000) and 2 hour (P=0.000) after the administration of the compounds. Pentazocine produced significant analgesic activity both at 1 hour (P=0.006) and at 2 hour (P=0.000).

The tail withdrawal time at baseline did not differ significantly between groups at baseline (P= 0.076). It differed significantly from each other at 1 hour (P= 0.017) and at 2 hour (P= 0.001) after the administration of the compounds. Pentazocine produced significant analgesic activity both at 1 hour and 2 hour (P= 0.008) as compared to control.

In acetic acid writhing test, the number of writhes in different groups was statistically different from each other (P = 0.000). Diclofenac significantly (P = 0.000) reduced the number of writhes as compared to control.

PC/CL/SWP05

In acetic acid writhing test, PC/CL/SWP05 at 100, 200 and 400 mg/kg doses significantly reduced the number of writhes as compared to control (P = 0.000). The compound did not produce significant activity in tail flick and tail immersion tests. This show PC/CL/SWP05 may have peripheral but not central analgesic activity.

CL/111107506

In acetic acid writhing test, CL/111107506, at all three doses significantly reduced the number of writhes as compared to control (P = 0.000). CL/111107506 at 100 mg/kg significantly increased the tail withdrawal time at 1 hour (P = 0.022). The compound did not produce significant activity in the tail flick tests.

PT/0606188

PT/0606188 at 200 and 400 mg/kg decreased the number of writhes as compared to control (P = 0.020, 0.000 respectively). PT/0606188 at 400 mg/kg increased the tail flick latencies at 1 hour as compared to control (P = 0.018). This compound did not show analgesic activity in tail immersion tests.

4. Discussion

There are a few studies, which demonstrate the analgesic effect of curcumin. Administration of a single dose, per orally of Curcumin at 100 and 200 mg/kg, 45 minutes prior to testing, significantly suppressed the latent phase of formalin induced pain [18]. This latent phase of formalin induced pain correlates with the inflammatory pain. It has been shown that curcumin inhibits cyclo-oxygenase pathway with COX-2 specificity [25]. This is postulated as one of the probable mechanisms for its analgesic activity in inflammatory pain.

In another study, chronic administration of curcumin at 20 and 40 mg/kg b. wt. increased the latency time to the beginning of the first writhe and reduce the total number of writhes counted for one hour, in acetic acid induced writhing test in mice [19]. This is in conjunction with our results, which shows that all the three extracts produce significant analgesic effect in acetic acid test. This suggests that all three extracts have significant peripheral analgesic activity.

There are no studies in the literature in which effect of curcumin on tail flick and tail withdrawal test have been performed. It has been reported that JCICM- 6, an herbal formula with Curcuma longa as one of its components, has produced significant analgesic activity in tail flick test on rats and acetic acid induced writhing reflex on mice [26].

Curcumin is postulated to have anti-nociceptive action by activation of both opioid and non-opioid pain mediating systems. It may exert its analgesic activity by inhibition of a number of different molecules that play a role in inflammation. In conclusion it seems several mechanisms are involved in the analgesic action of curcumin. Further studies are required to identify these mechanisms of action.

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