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ANTIPYRETIC AND ANALGESIC ACTIVITY OF *PICRORHIZA KURROOA* RHIZOMES

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ABSTRACT: *Picrorhiza kurroa* Royle ex Benth, belongs to the family Scrophulariaceae has gained immense medicinal value in Ayurvedic as well as in modern medicines including antioxidant, anti-inflammatory, anti-pyretic, immunomodulatory, anticancer, hepatoprotective, etc. The present study aimed to ascertain analgesic and antipyretic activities of rhizome extracts of *Picrorhiza kurrooa* in Wister rats. Methanolic extracts at 260 mg/kg as well as 520 mg/kg exhibited highly significant ($P < 0.01$) analgesic and antipyretic activity by oral dose for analgesic and rectal dose for antipyretic effects. Whereas hydroalcoholic extract showed significant effects at 520 mg/kg but not as good as that of methanolic extracts.

INTRODUCTION: *Picrorrhiza kurrooa*, an herbal medicinal plant belonging to *Scrophulariaceae* family with around 200 genera and 3000 species, found in the Himalayan regions of China, Pakistan, India, Bhutan and Nepal¹. The plant has been reported for their different pharmacological activities like antioxidant², anti-cancer³, immuno-modulatory⁴ anti-inflammatory⁵, hepatoprotective⁶. The rhizomes of *P. kurrooa* have been traditionally used to treat liver, respiratory tract disorders, indigestion problems, fever, pain and dyspepsia⁷. The chemical studies on the *P. kurrooa* rhizomes revealed the presence of iridoids, acetophenones, and cucurbitacins^{8, 9}. Pyrexia, algisia is associated with several pathological conditions. It has been reported that the bark of *Picrorhiza kurrooa* and *Azadirachta indica*, along with fruits of *Terminalia chebula*,

Terminalia bellirica, *Phyllanthus Emblica*, dried aerial parts of *Swertia chirayita* and leaves of *Tinospora cordifolia* and *Adhatoda vasica* in fermented combinations is found to be effective in the treatment of Jaundice and is taken orally with honey¹⁰. Many synthetic drugs available for the treatment of these conditions cause multiple unwanted effects. Several studies are ongoing worldwide to find natural healing agents with a better safety profile. The current safety was thus aimed at evaluating antipyretic, analgesic activities of methanolic extract and hydroalcoholic extract of rhizome¹¹.

MATERIALS AND METHOD:

Extraction: *Picrorrhiza* rhizomes were procured from Himalaya Herbal Store, Saharanpur (U.P.). The roots sample was identified from NISCAIR (National Institute of Science Communication and Information Resources), by Dr. H. B. Singh, Scientist F, and Head, Raw materials Herbarium and Museum, New Delhi, Reference no. NISCAIR/RHMD/Consult/-2009-10/1281/85. Shade-dried rhizome was powdered with the help of electric grinder and subsequently used for methanolic hot extraction using Soxhlet apparatus.

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Hydroalcoholic extract (Methanol: Water = 50:50) was also prepared by cold maceration. The percentage yield for methanolic and hydroalcoholic extract was 22.88% and 34.29% respectively.

Animals: Swiss Albino mice (18-22 g) and Wister rats (180-200 g) of either sex kept at laboratory Animal Centre of Institute of ASBASJSM College of Pharmacy, Bela, Ropar, Punjab. The experimental protocol was approved by the IAEC under the accession no. ASCB/IAEC/02/10/016 (05-06-2010). Animals were procured from Punjab University Chandigarh and NIPER, Mohali. The animals were kept in polypropylene cages (4 per cage) and maintained on balanced ration with free access to clean drinking water as per Committee for Control and Supervision of Experiments on Animals (CPCSEA). The rats fasted for 24 h and mice for 3-4 h before the experiment.

Screening of Antipyretic Activity:

Yeast Induced Pyrexia: For the assessment of analgesic activity male and female albino mice were reported for their reaction time. The Mice showing a reaction time of 10 sec to the thermal stimulus of 55 ± 1 °C were selected. The pyrexia was induced subcutaneously by injecting a suspension of brewer's yeast (15%) in normal saline. Then, the mice were divided into six groups of six animals in each group. Group, I served as a control which received 0.5 ml of normal saline solution only. The Group II was administered with paracetamol orally at a dose of 110mg/kg body weight and was kept as a positive control. Group III, IV, V, VI were administered with methanolic and hydroalcoholic extracts at doses 260 mg/kg and 520 mg/kg. The test substances were dosed orally (0 h), and rectal temperature was recorded at 1, 2, 3 and 4 h. The difference in temperature between 0 h and at the end of 4 hours was compared and analyzed¹².

Screening of Analgesic Activity:

Hot Plate Method: Group I served as a control which received 0.5 ml of normal saline solution only. Codeine (15 mg/kg, IP) was used as a standard for comparison. Group III, IV, V, VI were administered intraperitoneally with methanolic and hydroalcoholic extract at doses 260 mg/kg and 520 mg/kg. Mice were screened by placing them on a hot plate maintained at 55 ± 1 °C and recorded the reaction time in seconds for licking of hind paw or jumping. The mice which reacted within 15s and which did not show large variation when tested on four separate occasions were selected for studies. The time for hind paw licking or jumping on the heated plate of analgesimeter was taken as the reaction time.

Statistical Analysis: Student's t-test was employed for statistical analysis of the data. A probability value of less than 0.05 or 0.001 was considered statistically significant. Values in the text and tables are represented as mean \pm SEM.

RESULTS AND DISCUSSION:

Analgesic Activity:

Hot Plate Reaction time in Mice: The methanolic extract of *Picrorhiza kurroa* at doses of 260 mg/kg as well as 520 mg/kg exhibited highly significant ($P < 0.01$) analgesic activity. The hydroalcoholic extract of *Picrorhiza kurroa* also exhibited significant effects at 520 mg/kg but not so good as that of methanolic extract. Experimental groups were compared with control initially and after 30 min, 60 min, 90 min, 120 min. The time in seconds spend on hot plate increases with time.

The result given is mean \pm S.E.M number of animal used (n=6), ** $P < 0.01$ (highly significant), * $P < 0.05$ (significant), # $P > 0.05$ (not significant), Dunnett t-test was performed via Dunnett: Compare all vs. Control ANOVA **Table 1**.

TABLE 1: EFFECT OF THE MEPK AND HAEPK ON HOT PLATE REACTION TIME IN MICE

Drug	Dose (mg/kg), b.w mg(mg/kg), b.w	Reaction time in seconds at a time (min)				
		0	30	60	90	120
Control (normal saline)	-	4.40 \pm 0.25	5.05 \pm 0.37	4.26 \pm 0.38	4.95 \pm 0.29	4.76 \pm 0.48
Standard (Codeine)	30	3.51 \pm 0.29 [#]	7.63 \pm 0.32 ^{**}	8.37 \pm 0.32 ^{**}	9.14 \pm 0.23 ^{**}	9.46 \pm 0.29 ^{**}
HAEPK ₁	260	3.94 \pm 0.27 [#]	4.34 \pm 0.44 [#]	5.09 \pm 0.31 [#]	6.06 \pm 0.18 [*]	6.98 \pm 0.30 ^{**}
HAEPK ₂	520	3.55 \pm 0.43 [#]	4.93 \pm 0.48 [#]	5.58 \pm 0.25 [*]	6.69 \pm 0.41 ^{**}	7.35 \pm 0.52 ^{**}
MEPK ₁	260	3.54 \pm 0.16 [#]	5.17 \pm 0.29 [#]	5.55 \pm 0.23 [*]	6.98 \pm 0.13 ^{**}	7.52 \pm 0.22 ^{**}
MEPK ₂	520	3.74 \pm 0.38 [#]	5.67 \pm 0.26 [#]	6.04 \pm 0.21 ^{**}	7.36 \pm 0.30 ^{**}	7.95 \pm 0.41 ^{**}

Antipyretic Activity:

Yeast Induced Pyrexia in Rats: The MEPK at doses of 260 mg/kg as well as 520 mg/kg exhibited highly significant ($P < 0.01$) antipyretic activity. The hydroalcoholic extract of *Picrorhiza* also exhibited significant effects at 520 mg/kg but not so good as that of methanolic extract. Experimental groups were compared with control initially and after 1 h,

2 h, 3 h, and 4 h. There is a decrease in temperature. The results given are mean \pm S.E.M.; some animals used ($n = 6$), $**P < 0.01$ (highly significant) $*P < 0.05$ (significant), $\#P > 0.05$ (not significant), Dunnett t-test was performed *via* Dunnett: Compare all vs. Control ANOVA **Table 2**.

TABLE 2: EFFECT OF THE MEPK AND HAEPK ON INDUCTION OF YEAST INDUCE PYREXIA IN RATS

Drug	Dose (mg/kg), b.w	The rectal temperature in °C at the time (h)					
		-24 ^a	0 ^b	1	2	3	4
Control (normal saline)	-	38.40 \pm 0.24	39.05 \pm 0.30 (+0.65) ^c	39.41 \pm 0.28	38.83 \pm 0.30	38.86 \pm 0.21	38.73 \pm 0.24
Standard (PCM)	100	38.45 \pm 0.2	39.5 \pm 0.14 (+1.05) ^c	38.35 \pm 0.17 [*]	37.56 \pm 0.14 [*]	37.11 \pm 0.47 ^{**}	35.98 \pm 0.14 ^{**}
HAEPK ₁	260	38.11 \pm 0.32	39.56 \pm 0.27 (+1.45) ^c	39.21 \pm 0.23 [#]	38.85 \pm 0.24 [#]	38.31 \pm 0.23 [#]	37.85 \pm 0.23 [#]
HAEPK ₂	520	38.95 \pm 0.38	40 \pm 0.39 (+1.05) ^c	39.58 \pm 0.29 [#]	38.83 \pm 0.24 [#]	38.01 \pm 0.29 [*]	37.3 \pm 0.36 ^{**}
MEPK ₁	260	38.6 \pm 0.35	39.56 \pm 0.26 (+0.96) ^c	39.1 \pm 0.20 [#]	38.5 \pm 0.31 [#]	37.51 \pm 0.15 ^{**}	37.06 \pm 0.11 ^{**}
MEPK ₂	520	38.18 \pm 0.27	39.43 \pm 0.22 (+1.25) ^c	38.56 \pm 0.37 [#]	37.9 \pm 0.41 ^{**}	36.85 \pm 0.30 ^{**}	35.9 \pm 0.29 ^{**}

HAEPK = Hydroalcoholic extract of *Picrorhiza kurrooa* Royle ex Benth, MEPK = Methanolic extract of *Picrorhiza kurrooa* Royle ex Benth. HAEPK1 = Hydroalcoholic extract of *Picrorhiza kurrooa* Royle ex Benth at the dose of 260 mg/kg b.w., HAEPK2 = Hydroalcoholic extract of *Picrorhiza kurrooa* Royle ex Benth at the dose of 520 mg/kg b.w., MEPK1 = Methanolic extract of *Picrorhiza kurrooa* Royle ex Benth at the dose of 260 mg/kg b.w., MEPK2 = Methanolic extract of *Picrorhiza kurrooa* Royle ex Benth at the dose of 520 mg/kg b.w. a = temperature just before yeast injection, b = temperature just before yeast injection, c = change in temperature following yeast injection

CONCLUSION: The present study concluded that *Picrorhiza kurrooa* (rhizome) methanolic extracts at 260 mg/kg as well as 520 mg/kg exhibited highly significant analgesic and antipyretic effect. However, the exact phytochemical responsible for these effects of *Picrorhiza kurrooa* have to be identified, and further pharmacological studies may be taken up in developing lead compounds and to overcome the limitations of current work. In support to folklore claims for the cure of wounds, inflammation, pain and associated conditions where *Picrorhiza kurrooa* is used could be justifiable.

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