Analgesic activity of *Piper longum* Linn. root

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*Piper longum* root, commonly called Kandantippili, is traditionally used to treat rheumatism, insomnia, palisy and epilepsy. But a scientific study on its central actions is not available. This study screens *P. longum* root for opioid type analgesia using rat tail-flick method and for NSAID type analgesia using acetic-acid writhing method. Pentazocine (ip) and ibuprofen (oral) are used as respective drug controls. An aqueous suspension of *P. longum* root powder is given orally to mice and rat in doses of 200, 400 and 800 mg/kg. The delay in reaction time for thermal stimulus in rats and the number of writhings to chemical stimulus in mice are determined in each group. The results are analysed statistically. The 400 and 800 mg/kg doses of *P. longum* show significant NSAID type of analgesia (*P*<0.001). Both ibuprofen (40 mg/kg) and *P. longum* (800 mg/kg) show 50% protection against writhing. The delay in reaction time to thermal stimulus was less than 6% for different doses of *P. longum* as against 100% for pentazocine. This indicates that *P. longum* root has weak opioid but potent NSAID type of analgesic activity.

**Keywords**: Analgesic activity, Pentazocine, *Piper longum*, NSAID, Thermal stimulus

*Piper longum* Linn, is a traditional herbal remedy included in the poly-herbal formulations of Ayurvedic medicine17. The fruits and stem of the plant are referred as ‘tippilli’ while the root is popular as ‘kandantippilli’. Traditionally the fruits and root are used in palsy, gout, rheumatism, lumbago, bronchitis and as abortifacient4. Proper scientific studies have been conducted with *Piper longum* either as a whole plant or as fruits, stem or root. The whole plant as such has been reported to possess hypoglycemic, antispasmodic2, medullary stimulant3 and cough suppressant4 effects. While many scientific studies have identified the potential like anti-inflammatory activity5, anti-fertility activity10,11 and antiallergic activity12 in fruits, only limited data are available for the root. Only the antifertility potential of the root has been scientifically probed and reported10,11,13 so far. Hence this study on the analgesic potential of the *P. longum* root, referred as Kandantippili is undertaken.

Analgesic activity can be assessed by screening an agent for protection against pain stimulus applied to superficial (spinal) or deep (supraspinal) nociceptors. Agents that give positive results in tests involving spinal nociceptors (Rat tail flick method) are considered to have opioid type of analgesia while those involving supraspinal nociceptors (Acetic acid writhing method) signify NSAID type of analgesia14.

**Study design**

*Piper longum* root, procured locally and authenticated by Pharmacognosy Department of the Institution, was powdered and made into an aqueous suspension, using gum acacia as suspending agent, for oral administration. A pilot study to arrive at the minimum effective dose was done and based on this three graded doses, 200, 400 and 800 mg/kg were selected. The animals were housed in cages and maintained on standard pellet feed and free access to water in the animal house. The animals included in the study were deprived of food alone on the night prior to the day of testing and were divided into 5 groups. Each of these groups comprised 5 animals. The 3 test groups received one dose each (KT 200, KT 400 and KT 800), while the other two groups served as drug control and vehicle control respectively.

**Assessment of NSAID type of analgesia**

The method outlined by Koster et al.15 was followed. Mice of either sex weighing 18 to 25 g, that showed writhing within 3 to 5 min of intraperitoneal injection of 1% acetic acid, were selected for the study. On the day of testing, the animals were given either vehicle alone or the appropriate dose of *P. longum* root suspension or ibuprofen 40 mg/kg, orally16. The animals were constantly watched for writhing and the number of writhing exhibited by each animal within 20 min of treatment, was counted. The results were analysed by Student’s unpaired *t* test.

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Assessment of opioid type of analgesia

Rat tail flick method of D’Amour and Smith was followed. The rats of either sex weighing 150 to 200 g, that showed tail flick within 3 sec were selected by applying heat stimulus at 50°C, using Techno analgesiometer (Lucknow). The reaction time was noted down for all rats prior to treatment. Then the treatment with vehicle, or P. longum root suspension was given orally to respective groups. The drug control group (PENTA) received the standard dose of 10 mg / kg of pentazocine, intraperitoneally. The reaction time for the stimulus was noted down for all groups at 30 min intervals for 150 min. The results were analysed using Student’s paired t test.

NSAID type of analgesia

The number of writhing exhibited by mice in each group was noted down and statistically analysed (Fig. 1). The decrease in the number of writhing by ibuprofen, KT 400 and KT 800 groups are statistically significant (P<0.001) when compared to control group whereas that of KT 200 is not significant (P>0.05).

OPIOID analgesia

Figure 2 illustrates the delay in reaction time in rat tail flick method for control group and pentazocine treated groups. The control group did not show any change in reaction time throughout the observation period of 150 min. The pentazocine treated group showed maximum increase in reaction time with the peak analgesic effect at 30 min. Figure 2 also illustrates the results of various P. longum treated groups. Compared to control group there is only a slight increase in reaction time in these groups. The difference in reaction time before and after treatment at each time interval for each group was calculated and statistically analysed using Student’s paired ‘t’ Test. The results indicate that this difference is highly significant in pentazocine group (P<0.0001) when compared to P. longum treated groups (P<0.05).

The results are converted into % of Maximum Probable Effect (%MPE). In acetic acid writhing method the MPE is kept as 100 % protection against writhing and %MPE is calculated for all groups and plotted as in Fig. 1. The ibuprofen treated group and KT 800 treated groups are equipotent showing 50% protection. With KT 200 dose the % MPE is minimal but with KT 400 and KT 800 doses there is a dose

![Fig. 1 — NSAID type of analgesia: Acetic acid writhing in mice](image_url)

![Fig. 2 — Opioid analgesia: Rat tail flick method](image_url)

![Table 1 — Opioid analgesia by Piper longum root (Rat tail flick method)](table_url)
dependent increase in protection against writhing. In rat tail flick method the delay in reaction time by pentazocine, at each time interval, is kept as MPE (100% analgesia) and the %MPE for P. longum treated groups is calculated and tabulated (Table 1). The %MPE for P. longum treated groups is < 5% indicating that the analgesic activity of P. longum is no where comparable with that of pentazocine. The phytochemical study on P. longum root indicates the presence of an essential oil and two alkaloids namely piperlongumine and piperlonguminine. Various studies on the alkaloid piperlongumine from the root have not included screening for CNS activity. Therefore it is possible to speculate that the analgesic activity observed in this study may reside in one of the active principles mentioned above.

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References