The aim of this study was to investigate the analgesic and antipyretic properties of the ethanol extract of aerial part of *Neolitsea scrobiculata* in wistar albino rats. The analgesic activity of aerial part of *Neolitsea scrobiculata* was studied using hot plate method and tail immersion method in rats. The antipyretic activity of aerial part of *Neolitsea scrobiculata* was studied in Brewer’s yeast induced pyrexia in rats. In analgesic activity by hot plate and tail immersion models, ethanol extract significantly ($p<0.001$) reduced the painful stimulus. This confirms central and peripheral effects of the drug. It also possess antipyretic activity, ethanol extract significantly ($p<0.01$) reduced fever at higher doses within 3 hours on Brewer’s yeast induced pyrexia model in rats.

Keywords: Analgesic, Antipyretic, Diclofenac, *Neolitsea scrobiculata*, Pyrexia.

**Introduction**

Pain is an unpleasant sensation that is a consequence of complex neurochemical processes in the central and peripheral nervous systems [1]. Non-steroidal antiinflammatory drugs (NSAIDS) opioids are used in management of mild to moderate and severe pains respectively. These drugs have serious limitations due to their side effects. Opioids cause respiratory depression, euphoria, tolerance and dependence while non-steroidal antiinflammatory drugs produce gastrointestinal irritation and renal damage. Therefore, there is a need to intensify research with the aim of developing efficacious agents with low toxicity profile. Herbal medicine is still the mainstay of therapy for about 75-80% of the whole population in developing countries for primary health care. This is because of better cultural acceptability, affordability, better compatibility with the human body and lower side effects [2]. Pyrexia or fever is defined as an elevation of body temperature. It is a response due to tissue damage, inflammation, malignancy or graft
rejection. Cytokines, interleukin, interferon and tumor necrosis factor α (TNF-α) are formed in large amount under this condition, which increase PGE2 which in turn triggers hypothalamus to elevate body temperatures [3]. Fever is associated with symptoms of sickness behaviour which consists lethargy, depression, anorexia, sleepiness and inability to concentrate. This increase in set point triggers increased muscle bone and shivering. However, antipyretic medication can be effective at lowering the temperature which may include the affected persons comfort [4]. The genus *Neolitsea* or *Litsea* belongs to the family Lauraceae is a potential source of biological active compounds, such as flavonoids, butanolides, sesquiterpene, 1,3-diarylpropan-2-01, coumarin, syringaldehyde and essential oils. But no such literatures are revealed for its activity against treatment of diseases. However, no data are available in the literature on the analgesic and antipyretic activities of aerial part of *Neolitsea scrobiculata*. Therefore, the present investigation was undertaken to evaluate the analgesic and antipyretic activities of ethanol extract of *Neolitsea scrobiculata* aerial part.

**Materials and Methods**

**Collection of plant samples:** The aerial part of *Neolitsea scrobiculata* were collected from Kothagiri, Nilgiri Biosphere Reserve, Western Ghats, Tamil Nadu, India. The plant samples were identified with the help of local flora and authenticated by Botanical Survey of India, Southern Circle, Coimbatore, Tamil Nadu, India. A voucher specimen (VOCB4082) of collected plants was deposited in the Ethnopharmacological Unit, PG & Research Department of Botany, V.O. Chidambaran College, Thoothukudi District, Tamil Nadu.

**Preparation of plant extract for phytochemical screening, analgesic and antipyretic activities**

The aerial part of the plant was dried under shade and then powdered with a mechanical grinder to obtain a coarse powder, which was then subjected to extraction in a soxhlet apparatus using ethanol. The extract was subjected to qualitative test for the identification of various phytochemical constituents as per standard procedures [5,6,7]. The ethanol extract was concentrated in a rotary evaporator. The concentrated ethanol extract was used for analgesic and antipyretic activities.

**Animals:** Adult Wistar Albino rats of either sex (150-200g) were used for the present investigation. Animals were housed under standard environmental conditions at temperature (25±2°C) and light and dark (12:12 h). Rats were fed with standard pellet diet (Goldmohur brand, MS Hindustan lever Ltd., Mumbai, India) and water *ad libitum*. The experimental protocol was approved by the Institutional Animal Ethical Committee of Kongunadu Arts and Science College (Reg. No: 659/02/a CPSEA) Coimbatore, India.
Acute toxicity study: Acute oral toxicity was performed by following OECD-423 guidelines (acute toxic class method), albino rats (n=6) of either sex selected by random sampling were used for acute toxicity study [8]. The animals were kept fasting for overnight and provided only with water, after which the extracts were administrated orally at 5mg/kg body weight by gastric intubations and observed for 14 days. If mortality was observed in two out of three animals, then the dose administrated was assigned as toxic dose. If mortality was observed in one animal, then the same dose repeated again to confirm the toxic dose. If mortality was not observed, the procedure was repeated for higher doses such as 50,100 upto 2000 mg/kg body weight.

Evaluation of analgesic activity

Eddy’s hot plate method
The wistar albino rats were divided in to five groups of 6 animals each. Group I served as control. Group II served as standard and were injected Diclofenac (10 mg/kg) intraperitoneal. Group III, Group IV and Group V were treated orally with aerial part ethanol extracts of Neolitsea scrobiculata at the doses of 100 mg/kg, 200 mg/kg and 400 mg/kg body weight respectively. The rats were individually placed on the hot plate maintained at 55°C, one hour after their respective treatment. The response time was noted as the time at which rats reacted to the pain stimulus either by paw flicking or jump response, whichever appeared first. The cut off time for the reaction was 15 seconds.

Tail Immersion method
The wistar albino rats were divided into five groups of 6 rats each. Group I served as control. Group II served as standard and were injected Diclofenac (10 mg/kg) intraperitoneal. Group III, Group IV and Group V were treated orally with aerial part ethanol extracts of Neolitsea scrobiculata at the doses of 100 mg/kg, 200 mg/kg and 400 mg/kg body weight respectively. After one hour, the lower 5cm portion of the tail was immersed in a beaker of freshly filled hot water maintained at 55°C ± 1.0°C. The time taken to withdraw the tail was noted as reaction time. A cut of time of 10 seconds was maintained to prevent tissue damage. The time required for flicking of the tail was recorded to assess response to noxious stimulus [9].

Evaluation of antipyretic activity

Brewer’s yeast induced pyrexia method
The antipyretic activity was evaluated by using Brewer’s yeast induced pyrexia method in wistar albino rats. Fever was induced by injecting 2.0 ml/kg of 20% aqueous suspension of Brewer’s yeast in normal saline and 18 hour after yeast injection the test drugs were administrated. Rectal temperature was recorded by clinical thermometer at 0, 1, 2,
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3 and 6 hour after drug administration. The rats were divided into five groups of 6 animals in each and were given the following treatment orally. Group I (control) received 1% normal saline. Group II received indomethacin (10 mg/kg) as standard drug. Group III, IV and V received (100, 200 and 400 mg/kg) of ethanol extract of aerial part of Neolitsea scrobiculata. Before the experiment, the rats were maintained in separate cages with food *ad libitum* for 7 days and the rats with approximately constant rectal temperature (37.5 to 38.5°C) were selected for the study. The mean rectal temperature was found out for each group and compared into value of standard drug [9].

**Statistical analysis**

All values were expressed as mean ± SEM. The results were analysed for statistical significance using one-way ANOVA followed by Tukey Kramer multiple comparison test with ***p<0.001, **p<0.01 and *p<0.05 were considered as significant.

**Results**

**Preliminary phytochemical screening**

The preliminary phytochemical screening of the aerial part ethanol extract showed the presence of alkaloid, coumarin, catechin, flavonoid, steroid, saponin, glycoside, phenol, tannin, terpenoid and sugar.

**Acute toxicity**

Oral administration of the ethanol extract of Neolitsea scrobiculata aerial part did not cause any acute toxicity in experimental rats at all the tested dosages, confirming that it was potentially safe for consumption.

**Analgesic activity**

**Eddy's hot plate method**

Rats treated with ethanol extract of Neolitsea scrobiculata aerial part showed significant (p<0.001) and dose dependent analgesic activity in thermal stimulated pain (hot plate test) in rats. The reaction time at a dose of 400mg/kg (higher dose) was found to be 20.16 seconds after 90 minutes of drug treatment, whereas the standard drug diclofenac showed the tail flick latency17.54 seconds (Table 1).

**Table-1: Analgesic activity of ethanol extract of Neolitsea scrobiculata aerial part on the adult albino rats.**

<table>
<thead>
<tr>
<th>Treatment Groups</th>
<th>Response Time in sec ( Mean ± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Eddy Hot Plate Method</td>
</tr>
<tr>
<td>Group I</td>
<td>3.95±0.165</td>
</tr>
<tr>
<td>Group II</td>
<td>17.54±0.159***</td>
</tr>
<tr>
<td></td>
<td>Tail Immersion Method</td>
</tr>
<tr>
<td></td>
<td>2.92±0.026</td>
</tr>
<tr>
<td></td>
<td>12.96±0.118***</td>
</tr>
</tbody>
</table>
The data were expressed as mean ± S.E.M.; ANOVA followed by Tukey Kramer Multiple Comparison test: ***p<0.001, **p < 0.01 and *p<0.05 (Extracts vs. control)

**Tail Immersion method**

Rats treated with ethanol extract of *Neolitsea scrobiculata* aerial part showed significant (p<0.001) increase in the tail flick latency compared to control. The tail flick latency at a dose of 400mg/kg (higher dose) was found to be 15.16 seconds after 90 minutes of drug treatment, whereas the standard drug diclofenac showed the tail flick latency 12.96 seconds (Table 1). The activity was also found to be a significant activity.

**Antipyretic activity**

**Brewer’s yeast induced pyrexia method**

The results of antipyretic activity of ethanol extract of *Neolitsea scrobiculata* aerial part was shown in Table 2. Ethanol extract reduced the hyperthermic at 100, 200 and 400mg/kg doses after 1 hour after administration. The initial and final rectal temperature in the groups treated with ethanol extract (400mg/kg) and indomethacin (10 mg/kg) were 39.73±0.11°C and 34.04±0.36°C; 39.54±0.18°C and 34.16±0.13°C respectively. Both ethanol extract and indomethacin showed significant (p<0.001) antipyretic activity throughout the test period of 6 hour.

**Table-2: Effect of ethanol extract of *Neolitsea scrobiculata* aerial part on the Antipyretic activity in Brewer’s yeast induced pyrexia rats.**

<table>
<thead>
<tr>
<th>Treatment Groups</th>
<th>Rectal Temperature in °C after 18hrs of Yeast Injection (Mean± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-18hr</td>
</tr>
<tr>
<td>Group I</td>
<td>36.19±0.13</td>
</tr>
<tr>
<td>Group II</td>
<td>37.06±0.18</td>
</tr>
<tr>
<td>Group III</td>
<td>37.16±0.18</td>
</tr>
<tr>
<td>Group IV</td>
<td>37.38±0.13</td>
</tr>
<tr>
<td>Group V</td>
<td>37.65±0.18</td>
</tr>
</tbody>
</table>

Data expressed in mean ± SEM; Level of significance: * P < 0.05 when compared to control. ** P < 0.01 **p<0.01 when compared to control
a Temperature just before yeast injection

b Temperature just before drug administration

**Discussion**

Results of the present study showed that *Neolitsea scrobiculata* has marked analgesic and antipyretic affects with a reasonable safety profile.

Thermal nociception models such as hot plate and the tail immersion test were used to evaluate central analgesic activity. *Neolitsea scrobiculata* showed significant (\(p<0.001\)) analgesic effect in both the hotplate and tail immersion test, implicating both spinal and supraspinal analgesic pathways. In these pain paradigms diclofenac, which is similar to the action of opioid agonists raised the pain threshold level. In contrast, *Neolitsea scrobiculata* showed maximum analgesic effect after 90 min of administration. This difference in the maximum analgesic point could be explained by difference in the metabolic rate of each drug or may be the potency of each drug as the analgesic potential of diclofenac is lesser than *Neolitsea scrobiculata* (400mg/kg). A number of flavonoids have been reported to produce analgesic activity. Also, there are few reports on the role of tannins and alkaloids in analgesic activity [10,11]. Hence, the present analgesic activity of *Neolitsea scrobiculata* aerial part may be attributed due to the presence of alkaloids, flavonoids and tannins.

Subcutaneous injection of Brewer's yeast induces pyrexia by increasing the synthesis of prostaglandin. It is considered as a useful test for the screening of plants materials as well as synthetic drugs for their antipyretic effect [12,13,14]. Yeast induced pyrexia is called pathogenic fever and its etiology could be the production of prostaglandins [15]. The inhibition of prostaglandin synthesis could be the possible mechanism of antipyretic action as that of paracetamol and the inhibition of prostaglandin can be achieved by blocking the cyclo-oxygenase enzyme activity. There are several mediators that are responsible for the antipyretic effect [16].

The administration of ethanol extract of aerial part of *Neolitsea scrobiculata* significantly attenuated rectal temperature of yeast induced rat. Thus it can be postulated that *Neolitsea scrobiculata* contained pharmacologically active principle(s) that interfere with the release of prostaglandins.

The phytochemical analysis of the ethanol extract of *Neolitsea scrobiculata* aerial part showed the presence of alkaloids, flavonoids, phenols, tannins, saponins and steroids. The flavonoid present in the ethanol extract of *Neolitsea scrobiculata* may also be responsible for its antipyretic activity by inhibiting prostaglandian synthesis in hypothalamus [17]. In many earlier studies, flavonoids have been reported to exhibit antipyretic effect [18,19,20].
Hence, the presence of flavonoids in the ethanol extract of *Neolitsea scrobiculata* may be contributory of its antipyretic activity.

**Conclusion**

This study confirmed the biological significance of the ethanol aerial part extract of *Neolitsea scrobiculata* in terms of its potent analgesic and antipyretic activities. These findings conclude that the ethanol aerial part extract of *Neolitsea scrobiculata* may contain bioactive principles with pharmacological potential. However, further investigation is required to isolate the active constituents responsible for these activities and to elucidate the exact mechanism of action.

**References**


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