SCREENING OF ANTINOCICEPTIVE ACTIVITY OF EUPHORBIA FUSIFORMIS BUCH-HAM

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ABSTRACT
Antinociceptive activity of Euphorbia fusiformis root powder was investigated using acetic acid writhing, tail flick and formalin induced paw licking tests. The test was performed at two dose levels in Swiss albino mice and Wistar strain albino rats. Oral administration of Euphorbia fusiformis root powder did not produce any significant effect on acetic acid induced writhings, however in tail flick test it significantly raised pain threshold at both dose levels and is prolonged. Moreover, at high dose level it significantly inhibited the formalin induced paw licking responses at both the phases. The result of pharmacological tests performed in the present study suggests that Euphorbia fusiformis root possesses potent analgesic property which is mediated via central inhibitory mechanism. This could provide a rationale for the use of this plant in treatment of rheumatism in folk medicine.

KEYWORDS: Euphorbia fusiformis, Tail flick, Writhing, Analgesic, Formalin

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INTRODUCTION
Plants and plant based medicaments have been employed since the dawn of civilization for prolonging life of man by combating various ailments. Indigenous people living on their traditional territory largely rely on medicinal plants for healthcare and they are therefore rich in ethnopharmacological knowledge. However, the meticulous scientific research is needed to evaluate their effectiveness in treatment of various diseases. Euphorbia fusiformis Buch.-Ham. Ex. D.Don (Euphorbiaceae) is a rare medicinal plant found in Tropical Himalaya up to 1500 ft. from Garhwal to Nepal and also found in Konkan and Deccan Hills1. In Gujarat sate it is found in Dangs, Rajpippala, Chotudaipur regions2. The ethnobotanical value of the plant refers to its recognized action as a remedy for several diseases like rheumatism, gout, paralysis and arthritis3,4. The tribals of Waghai and adjacent forest regions of Dansg district of Gujarat are ethnic people who dwell in the forests. The majority of these tribal people have their own method of treatment for various diseases. They have their own physician called Bhagat who knows ample of information regarding the medicinal herbs of forests, especially their proper identification and utilization. The Bhagats use Euphorbia fusiformis drug in the name of Ghate for treatment of various abdominal disorders especially for tumors of abdomen. They also use tuberous root of this plant in the form of paste for application in rheumatism. In spite of its reputation in treating ailments like rheumatism, till date no pharmacological screening to support its analgesic activity has been reported. Hence the present study was under taken to evaluate analgesic activity of roots of Euphorbia fusiformis in experimental animals.

MATERIALS AND METHODS
Test Drug
The tuberous roots of Euphorbia fusiformis Buch-Ham. (Family - Euphorbiaceae) was identified with the help of Taxonomist and collected from Waghai forest in fully matured condition. The tuberous roots were made into

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Pentazocine (20 mg/kg) was used. Refer similar to the effect of drug on incidence and number of writhing syndrome after the injection of acetic acid for a hour later. Mice were administered to overnight fasted animals and with aspirin (20 mg/kg p.o.). Second and third groups were administered with the test drug TED (Therapeutically equivalent dose) and TED × 2 (180 mg/kg for rat and 260 mg/kg for mouse). The test drug was suspended in tap water and administered orally to animals. The writhing syndrome is characterized by intermittent contraction of abdominal muscles, extension of hind limbs and twisting of trunk. Effect of drug on incidence and number of writhing syndrome was noted.

Radiant Heat Test

The animal groupings and test drug administration were similar to acetic acid induced writhing test, except the reference standard drug in this test Pentazocine (20 mg/kg) was used. The latency of tail flick response (TFL) was measured with the help of tail flick analgesiometer (INSIF-Ambala). Basal reaction time of animals to radiant heat was recorded by placing the tip (last 1-2 cm) of the tail on the radiant heat source. The tail withdrawal from the heat (TFL) is taken as the end point. A cut off period of 15 sec was observed to avoid damage to the tail. To obtain baseline value the tail flick response was measured three times in each animal initially. Then the test drugs were administered to respective groups and tail flick response was recorded at 30, 60, 120, 180 and 240 minutes.

Radiant Heat Test

Acetic Acid Induced Writhing Test

Swiss albino mice of either sex were grouped into four groups of 6 mice each. To the first group tap water was administered to serve as control. Second and third groups were administered with the test drug TED (130 mg/kg) and TED × 2 (260 mg/kg) respectively. The fourth group was taken as reference standard group and administered with aspirin (20 mg/kg p.o.). The test drugs were administered to overnight fasted animals and exactly one hour later acetic acid in the dose of 10 ml kg⁻¹ (3% v/v Solution) was injected intraperitoneally to each mouse. Analgesic effect was recorded by counting the number of writhing syndrome after the injection of acetic acid for a period of 30 minutes. The writhing syndrome is characterized by intermittent contraction of abdominal muscles, extension of hind limbs and twisting of trunk. Effect of drug on incidence and number of writhing syndrome was noted.

DISCUSSION

The present study was carried out to evaluate antinociceptive activity of *Euphorbia fusiformis* (Euphorbiaceae) root powder in different models of pain. The mechanism for testing analgesic was selected such that both centrally and peripherally mediated effects were investigated. The acetic acid induced abdominal constriction and tail flick methods elucidated peripheral and central activity, respectively, while the formalin test investigated both. In the acetic acid induced writhing model the constrictions induced by acetic acid in mice results from an acute inflammatory reaction with production of PGE2...
and PGF2α in the peritoneal fluid. Administration of test drug at both dose levels failed to inhibit acetic acid induced writhings, this may be due to lack of prostaglandin inhibitory effect.

Tail flick model which is thermal induced nociception indicates narcotic involvement which is sensitive to opioid μ receptors which focuses mainly on changes above the spinal cord level. The significant increase in pain threshold produced by Euphorbia fusiformis at both doses suggests involvement of central pain pathways. An important feature of the formalin test in rodents is that animals show two phases of antinociceptive behavior. The first phase (0 – 10 min) which is neurogenic and result of direct stimulation of nociceptors measure centrally mediated effects and is insensitive to anti-inflammatory agents while the second phase (20 – 30 min) is of inflammatory origin which is dependent on peripheral inflammation and changes in central procession due to chemical mediators release from damaged cells. Drugs with analgesic effect may inhibit or decrease the paw licking in both or either of the phases. Euphorbia fusiformis only at high dose level significantly inhibited the formalin induced paw licking responses at both the phases so as indomethacin which is a non-selective cyclooxygenase inhibitor. Further, ability of Euphorbia fusiformis root powder to inhibit both the phases of formalin induced pain response in addition to tail flick latency further indicates the involvement of central opioidergic mechanisms as the antinociceptive activity.

CONCLUSION
The results obtained in this study indicate that Euphorbia fusiformis root possesses potent analgesic property, which is mediated via central inhibitory mechanism. This could provide a rationale for the use of this plant in treatment of rheumatism in folk medicine.

REFERENCES

Table 1: Effect of Euphorbia fusiformis on acetic acid writhing syndrome

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of writhing episodes</th>
<th>% inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>32.66 ± 6.51</td>
<td>--</td>
</tr>
<tr>
<td>E. fusiformis (130mg/kg)</td>
<td>33.33 ± 6.60</td>
<td>--</td>
</tr>
<tr>
<td>E. fusiformis (260mg/kg)</td>
<td>31.83 ± 5.02</td>
<td>02.54</td>
</tr>
<tr>
<td>Aspirin (20mg/kg)</td>
<td>17.33 ± 1.54*</td>
<td>46.93</td>
</tr>
</tbody>
</table>

* P< 0.05 (Compared with control group)

Table 2: Effect of Euphorbia fusiformis on tail flick response

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Initial TFL (sec.)</th>
<th>TFL after drug administration (sec.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 min</td>
<td>60 min</td>
</tr>
<tr>
<td>Control</td>
<td>3.67 ± 0.42</td>
<td>3.11 ± 0.20</td>
</tr>
<tr>
<td>E. fusiformis (130mg/kg)</td>
<td>2.98 ± 0.43</td>
<td>2.71 ± 0.19</td>
</tr>
<tr>
<td>E. fusiformis (260mg/kg)</td>
<td>3.42 ± 0.38</td>
<td>3.68 ± 0.34</td>
</tr>
<tr>
<td>Pentazocine (20mg/kg)</td>
<td>2.10 ± 0.20</td>
<td>8.50 ± 0.79</td>
</tr>
</tbody>
</table>

** P< 0.01, ***P < 0.001 (Compared with control group)

Table 3: Effect of Euphorbia fusiformis on formalin induced paw licking response

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of paw lickings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-10 min</td>
</tr>
<tr>
<td>Control</td>
<td>12.16 ± 1.35</td>
</tr>
<tr>
<td>E. fusiformis (90mg/kg,po)</td>
<td>11.66 ± 0.84</td>
</tr>
<tr>
<td>E. fusiformis (180mg/l)</td>
<td>8.16 ± 1.04*</td>
</tr>
<tr>
<td>Indomethacin (10mg/kg)</td>
<td>08.33 ± 0.67*</td>
</tr>
</tbody>
</table>

* P< 0.05, **P < 0.01 (Compared with control group)