ANTI-INFLAMMATORY AND ANTINOCICEPTIVE ACTIVITY IN THE HERBAL DRUG AUJAIE

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ABSTRACT
Aujaie is a herbal product used for the treatment of arthritic condition. An investigation has been carried out to determine its anti-inflammatory and antinociceptive activity on mice. The results show that Aujaie significantly and dose dependently inhibit carrageenan-induced paw oedema as well as acetic acid induced writhing response. The effects are comparable to Indomethacin.

INTRODUCTION
The inflammatory diseases are much more common and create a major health problem among people, in which arthritis is the number one crippling disease all over the world. Today it’s so widespread that one in six people and one in three families are affected by it. It is estimated that arthritis affects approximately 80% of people in United States (Eidelson, 2004) and about 60% of the population in Pakistan and India (Ahmad, 2004).

There are many severe forms of arthritis with a known cause is gout, which is due to the disorder of purine metabolism associated with hyperuricemia and may lead to crippling of joints and uric acid urolithiasis. Osteoarthritis is another form of arthritis and is supposed to be a normal part of aging whereas, many other aggressive and crippling forms including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and systemic lupus are grouped together as inflammatory arthritis but their cause is generally held to be unknown.

Nowadays several NSAIDs are available that play major role in the treatment of arthritis but cause severe complications like renal and hepatic abnormalities, metabolic disturbances and concomitant disease such as arterial hypertension or type 2 diabetes mellitus (Barskova et al., 2004). For this purpose it is expedient to use that drug which is safer with least side effects.

Aujaie is one of the herbal product prepared by Hamdard Laboratories (Waqf) Pakistan, believed to have the potential for providing relief to joint pain (arthritis with or without the swelling of joints), gout, lumbago, sciatica and stiffening of joints and also helps in the excretion of uric acid.

This product is prepared from nine different plants and most of them have medicinal value in traditional medicine for treating rheumatism and gout such as Balsamodendron mukul is very potent for various types of joints problems like rheumatoid arthritis, osteoarthritis and gout and used in reducing pain, swelling and tenderness of inflammatory joints (Vatsyayan, 2001). Khan et al (1997) reported that Colchicum luteum, Curculigo orchioides and Zingiber officinalis possess antirheumatic, antigout and anti-inflammatory actions. Ptychotis ajowan relieves rheumatic and neuralgic pain (Chopra et al, 1956). Pistacia lentiscus is resolvent of inflammations and Withania somuifera is useful in rheumatoid
Anti-inflammatory and Antinociceptive Activity

arthritis, rheumatic fever, reduces the discomfort associated with arthritis, and also used to prevent tumors and inflammations (Said et al., 1996). The properties of these plants cannot determine the pharmacology of the product as such. So in order to understand the pharmacological basis for the treatment of inflammatory diseases of the product Aujaie, the present study was design to investigate the anti inflammatory as well as antinociceptive activity in mice.

MATERIALS AND METHODS

Animals and drugs
Mice of NMRI strain of either sex, weighing 25-30g were taken from Dr. HMI Institute of Pharmacology and Herbal Sciences. All animals had free access to water at all times. The following chemicals were used: Indomethacin B.P. (Indobid, manufactured by Adamjee Pharmaceuticals (Pvt.) Ltd.), glacial acetic acid (Scharlau Chemie S.A. Spain) and carrageenan (Sumbrph Company, Philippine).

Experimental Models
For both experiments mice were divided into six groups and each group contained six mice, where one of the group acted as control.

Table 1
Effect of Aujaie on carrageenan - induced paw oedema in mice

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean paw zone of inflammation (cm ± S.E.M)</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 hour</td>
<td>3 hour</td>
</tr>
<tr>
<td>Control</td>
<td>0.2280 ± 0.01</td>
<td>0.2376 ± 0.006</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>0.0932 ± 0.01</td>
<td>0.0975 ± 0.008</td>
</tr>
<tr>
<td>Aujaie 60mg/kg</td>
<td>0.2138 ± 0.004</td>
<td>0.2244 ± 0.007</td>
</tr>
<tr>
<td>Aujaie 120mg/kg</td>
<td>0.1921 ± 0.01</td>
<td>0.1999 ± 0.007</td>
</tr>
<tr>
<td>Aujaie 180mg/kg</td>
<td>0.1154 ± 0.003</td>
<td>0.1321 ± 0.007</td>
</tr>
<tr>
<td>Aujaie 240mg/kg</td>
<td>0.0955 ± 0.01</td>
<td>0.1053 ± 0.005</td>
</tr>
</tbody>
</table>

Oedema is expressed as increase in mean paw zone of inflammation ± S.E.M. n=6, values refer to % inhibition in paw zone of inflammation compared to control, at each time point.
In all cases, P<0.05: statistically significant relative to control.

Anti-inflammatory Activity

Effect of Aujaie on carrageenan - induced paw oedema
This method was determined as described by Winter et al. (1962). The drug Aujaie of doses (60,120, 180 and 240mg/kg), Indomethacin (4mg/kg) and distilled water were administered orally in all the divided groups. After 1 hour, oedema was induced in all the animals by injecting freshly prepared 0.1 ml of 1% suspension carrageenin in saline solution, into the plantar surface of right hind paw. The zone of inflammation was measured at 1 hour, 3 hour and 5 hour after induction of inflammation using vernier caliper (Razi et al., 2003). Oedema was expressed as the increment in paw thickness due to carrageenin administration.

Antinociceptive Activity

Writhing Test
Acetic acid induced writhing test was used to measure antinociceptive activity according to the previously described procedure of Bentley et al (1983). Test drug Aujaie, control vehicle (distilled water) and reference drug (indomethacin) were administered orally to NMRI mice at the above indicated doses, 1 hour prior to acetic acid injection. Acetic acid at the dose of 0.1 ml/10 g body weight was administered
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Statistical Analysis

Intraperitoneally and the number of writhes were counted for 30 min.

Data from evaluation of the product Aujaie in the carrageenan induced paw oedema was statistically analyzed using two-way ANOVA (P<0.05 was considered as the level of significance), while Student’s t-test was used for the comparison of means between control and experimental group in acetic acid -induced writhing reflex, where P<0.005 was considered as a level of significance.

RESULTS

Carrageenan - induced paw oedema

As apparent from Table 1, Aujaie could significantly (P<0.05) and dose dependently inhibit the carrageenan-induced paw oedema in mice. An inhibitory effect of Aujaie at the dose of 240 mg/kg was similar to that demonstrated by the reference drug Indomethacin.

Writhing test

The effect of Aujaie on the writhing response in mice is shown in Table 2. It was found that the increase in the doses of Aujaie

Table 2

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Treatment</th>
<th>Dose (mg/kg, p.o.)</th>
<th>Number of writhes</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>-</td>
<td>87.5 ± 7.24</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>Indomethacin</td>
<td>4</td>
<td>15.6 ± 1.54</td>
<td>82.17</td>
</tr>
<tr>
<td>3</td>
<td>Aujaie</td>
<td>60</td>
<td>64.16 ± 6.73</td>
<td>26.67</td>
</tr>
<tr>
<td>4</td>
<td>Aujaie</td>
<td>120</td>
<td>39.33 ± 4.83</td>
<td>55.05</td>
</tr>
<tr>
<td>5</td>
<td>Aujaie</td>
<td>180</td>
<td>20.66 ± 1.37</td>
<td>76.38</td>
</tr>
<tr>
<td>6</td>
<td>Aujaie</td>
<td>240</td>
<td>16.5 ± 2.37</td>
<td>81.14</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.E.M. in all cases P<0.005 compared to control.
anti-inflammatory and antinociceptive activity. 80% inhibition was seen at the dose of 240mg/kg of Aujaie which is comparable to the reference drug Indomethacin.

**DISCUSSION**

The present study shows that Aujaie has been demonstrated to possess significant anti-inflammatory and antinociceptive activity with dose dependent manner. An inhibitory effect was seen at 1 hour after carrageenan injection, which is attributed to the release of histamine and serotonin (Vinegar et al., 1969). A marked inhibition of oedema formation was also observed at the third and fifth hour, suggesting an inhibition of the release of kinins or cyclooxygenase, one of the enzyme involved in the formation of prostaglandin that induced the inflammation process (Di Rosa et al., 1971).

The antinociceptive activity of Aujaie was also evaluated using the writhing test in mice. Acetic acid, which is used the writhing syndrome, causes algesia by liberation of endogenous substances, which then excite the pain nerve endings. Aujaie was found to exert a significant inhibitory activity on writhing response in dose range of 60-240mg/kg. It is therefore concluded that Aujaie play a vital role in the treatment of inflammation. Aujaie upto the dose of 300 mg/kg/p.o. in mice and about 6000 mg/kg/p.o. in rats did not produce any toxic symptoms. Further experimentation is needed in order to understand the precise mechanism of action and it is worthwhile to test its anti-inflammatory and antinociceptive activity in other experimental models.

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