046A

Antinociceptive action of aqueous extract of the leaves of *Ixora coccinea*

W D Ratnasooriya[1*], S A Deraniyagala[2] S D N K Bathige[2] J R A C Jayakody[1], G Galhena[1] and S S P Liyanage[1]

[1]*Dept of Zoology, University of Colombo, P.O.Box 1490, Colombo*

[2]*Dept of Chemistry, University of Colombo, P.O. Box 1490, Colombo*

The water extract of *Ixora coccinea* (Family: Rubeaceae; Sinhala: Rathmal, Tamil: Vedchi) was obtained by refluxing mascerated fresh leaves in distilled water for two days. Different doses of extract (ALE) (500,750,1000 or 1500 mg/ kg; N= 8/group) or vehicle (1 mL distilled water) or meparadine (25 mg/ kg, i, m., positive control) were orally administered to male rats and the analgesic potential evaluated using three models of nociception (tail flick, hot plate and formalin tests).

The results show for the first time that the ALE possesses marked and dose-dependent antinociceptive activity as evaluated from hot plate and formalin tests but not tail flick test. Lack of motor deficiencies and presence of dose-dependent activity suggests that the ALE-induced antinociception was genuine and possibly receptor mediated. The positive result in the hot plate test suggest that the ALE-induced antinociception is mediated centrally as it is effective against acute phasic nociceptive pain. The ALE-induced inhibition of the early phase of formalin test provides additional support for this inference. Impairment of the late phase of formalin test indicates that the ALE is effective against continuous inflammatory pain, possibly by inhibiting release and/ or activity of inflammatory mediators. However, the ALE did not inhibit prostaglandin synthesis. ALE was nonstressogenic and antinociception due to stress can be ruled out. Antinociception activity of the ALE was not mediated *via* sedation as none of the parameters in the rat hole-board test was altered. The ALE also failed to inhibit heat-induced haemolysis of rat erythrocytes *in vitro*. Thus, the antinociception is unlikely to be due to membrane stabilizing effect and/ or raising of nociception threshold. The ALE did not induce Straub's tail reaction, CNS stimulating behaviors or marked breathing depression. The aninociception action of the ALE was not blocked by nalaxone, an opioid receptor antagonist. Collectively, these data indicates that antinociception is mediated independent of opioid mechanisms. In contrast, dopamine receptor antagonist, metachlorpromide, markedly attenuated the antinociception induced by the ALE suggesting that the antinociception is mediated primarily via dopaminergic mechanisms.

In addition, antioxidant activity of ALE may also play a role in producing antinociception. Chemical investigations showed the presence of quaternary base alkaloids and different polyphenol and flavonoids which may be linked with the antinociception of ALE. The former group can be linked with dopamine agonist activity and the later linked antioxidant activity of ALE. Some dopamine agonists such as apomorphine, selegiline, entacaporn possess tertiary nitrogen which could exist as quaternary salts in combination with plant acids.

Tel: 011 2503399