

ABSTRACT

We studied the effects of acute and chronic administration of aqueous neem leaf extract on the cardiovascular system in male Wistar rats with DOCA-salt induced hypertension.

For the acute experiments, rats were divided into Normal, Vehicle Control and DOCA-salt groups. In Normal rats, intravenous administration sequentially of 5, 10, 20, 40, 80 and 100 mg/kg body weight of neem extract caused significant fall in systolic, diastolic, mean arterial pressure, pulse pressure and in heart rate at all dosages above 20 mg/kg.

Blood Pressure in DOCA-salt treated rats was significantly higher than in Controls. Intravenous administration of 40 mg/kg of extract caused significant fall in blood pressure in Control and DOCA-salt groups. The effects of 40 mg/kg neem were similar to the effects of 5 μ g/kg acetylcholine and were blocked by 1 mg/kg atropine ($p < 0.05$).

Aortic rings from Control and DOCA-salt groups contracted at lower, but, in the DOCA-salt group relaxed markedly ($p < 0.05$) at higher bath concentrations of neem extract, with no significant difference in EC_{50} between groups. Removal of endothelium significantly attenuated the contractile responses ($\uparrow EC_{50}$) and abolished the relaxation responses in the DOCA-salt group.

Chronic administration of neem extract during DOCA-salt treatment (DOCA-salt-neem group) prevented blood pressure elevation, although Baroreflex Sensitivity was similarly depressed in both the DOCA-salt and the DOCA-salt-neem groups ($p < 0.05$).

Aortic rings from DOCA-salt rats were significantly more sensitive to noradrenaline and 5-HT than those from Controls and DOCA-salt-neem groups. Rings from DOCA-salt and DOCA-salt-neem rats showed significantly attenuated relaxation in response to acetylcholine. The DOCA-salt-neem rings in addition showed a contractile response at higher concentrations. TEA blockade of K_{Ca2+} channels attenuated ACh-induced relaxation in Control and DOCA-salt rings, but enhanced relaxation in DOCA-salt-neem rings and abolished the contractile response, virtually abolishing the difference between the Control and the DOCA-salt-neem groups.

Our results show that aqueous neem extract reduces blood pressure acutely in control and hypertensive rats perhaps by a cholinergic mechanism, and chronically, prevents the development of hypertension. Paradoxically, the acute effect of extract on isolated aortic smooth muscle was contractile at lower doses, relaxation appearing only at high concentrations.