Effect of harmalol on blood pressure in anaesthetized rats.

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Peganum harmala L. (Family: Zygophyllaceae; Local name: harma) is commonly found in Indo-Pak subcontinent and other parts of Asia [1]. Its seeds are narcotic, anthelmintic, antispasmodic and employed in cases of asthma and rheumatism in the indigenous system of medicine [2]. Recent investigations have revealed that main alkaloids, harmine, harmaline and tetrahydroharmine, which belong to category of hallucinogenics, are also potent reversible inhibitors of monoamine oxidase [3]. Further, alkaloids of P. harmala were found to possess antimicrobial activity [4]. Harmala alkaloids (harmine and harmaline) have been reported to possess coronary dilator, protozoecidal and hypotensive activities [5,6]. Harmalol prepared by demethylation of harmaline [7] has been used therapeutically as anthelmintic and narcotic [8], however, it has not been studied for its effect on blood pressure. The present study describes effect of harmalol on blood pressure in anaesthetized normotensive rats.

Wistar rats of either sex (200-250 g) were anaesthetized with pentothal sodium (50 mg/kg, i.p.). Trachea was exposed and cannulated to facilitate spontaneous respiration. The systemic blood pressure was recorded from the carotid artery via the arterial cannula connected to a pressure transducer (FT 03) and the responses were displayed on Grass model 79 polygraph. Drugs were slowly injected via the cannula inserted into external jugular vein. The maximum volume of injection was 0.2 ml. The animal was allowed to equilibrate for at least 30 min before administration of any drug. Mean blood pressure (BP) was calculated as the diastolic blood pressure plus one third of pulse width. Changes in blood pressure and heart rate expressed as % of control values obtained immediately before the administration of test substance(s).

In normotensive anaesthetized rats, intravenous administration of harmalol (1-10 mg/kg) produced a dose-dependent fall in blood pressure and heart rate (Fig. 1). Both the inhibitory effects were brief returning to normal within two minutes. Hypotensive and bradycardic effects of harmalol were qualitatively similar to that of acetylcholine which produced similar effects at 1 ug/kg (Fig 1). Pretreatment of animals with atropine (1 mg/kg) completely abolished the inhibitory cardiovascular responses of acetylcholine whereas responses to harmalol remained unaltered indicating that harmalol mediates hypotensive and bradycardic effects through a mechanism(s) different from that of acetylcholine. Administration of noradrenaline (1 ug/kg) produced strong vasoconstriction (data not shown). Pretreatment of animals with harmalol did not modify vasoconstrictor responses to noradrenaline which suggests that inhibitory responses of harmalol are independent of adrenoceptors blockade. Histamine is also known to cause vasoconstriction [9]. Though harmalol was not tested in the presence of histamine receptor blocking drugs but involvement of histaminergic mechanism is unlikely as histamine also produces increase in heart rate contrary to harmalol that produces bradycardia. However, further studies are required to explore exact mechanism of action.