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PHARMACOLOGICAL EFFECTS OF *AZADIRACHTA INDICA* (NEEM) LEAF EXTRACT ON THE ECG AND BLOOD PRESSURE OF RAT

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Abstract: Neem leaf alcoholic extract (NLE) was investigated for its effects on the ECG and blood pressure of rat. Intravenous administration of NLE (100, 300 and 1000 mg/kg) resulted in initial bradycardia followed by cardiac arrhythmia in rats. NLE produced a significant and dose-related fall in blood pressure which was immediate, sharp and persistent. Pre-treatment with either atropine or mepyramine failed to prevent the hypotensive effect of NLE.

Key words: Neem leaf alcoholic extract ECG blood pressure

INTRODUCTION

Azadirachta indica (neem) is a plant which is reported to possess several medicinal properties. Both aqueous and alcoholic extract of the stem bark, root bark and leaves have been used for the treatment of malaria, fever, jaundice and skin diseases like ulcers, urticaria and eczema (1, 2, 3). Aqueous extract of leaves possess hypoglycaemic and antihyperglycaemic effects (4). *A. indica* leaf and bark extract was found to have a pronounced anti-inflammatory (rat paw oedema) and fairly good antipyretic effect (5).

The present study was undertaken to find out the effect of neem leaf alcoholic extract on the ECG and blood pressure of anaesthetized rats.

METHODS

To study the effect of NLE on ECG, healthy male albino rats (300-350 g) were anaesthetized with pentobarbitone sodium (40 mg kg^{-1}, i.p.) and the jugular vein was cannulated. ECG was recorded on Polyrite (INCO) using lead II before and following i.v. administration of NLE in a dose of 100, 300 and 1000 mg kg^{-1} body weight.

To study the effect on B.P., the carotid artery of anaesthetized rats was cannulated and connected to a pressure transducer of a blood pressure monitor (CAVITRON-KDC). The normal blood pressure was recorded. Control responses of adrenaline (5 mg kg^{-1}), acetylcholine (5 µg kg^{-1}), histamine (5 mg kg^{-1}), atropine sulphate at 1 mg kg^{-1}, i.v. (10 min before test drug) and mepyramine maleate at 3 mg kg^{-1}, i.v. (10 min before test drug) were also recorded. Subsequently, NLE (1% aqueous solution) was administered i.v. in a dose of 100, 300 and 1000 mg kg^{-1}.

RESULTS AND DISCUSSION

Effect of NLE on the ECG: NLE (100 mg kg^{-1}, i.v.) reduced heart rate from 360/min to about 300/min (Fig. 1-A and B). At a higher dose of 300 mg kg^{-1}, the bradycardia was also associated with increase in P-R interval and missing of beats in the ECG (Fig. 1-C). At the dose level of 1000 mg kg^{-1}, NLE caused absence of P-wave, bradycardia and ventricular arrhythmia characterized by extra-systoles having bizarrely shaped, prolonged and inverted QRS complexes (Fig. 1-D and E).

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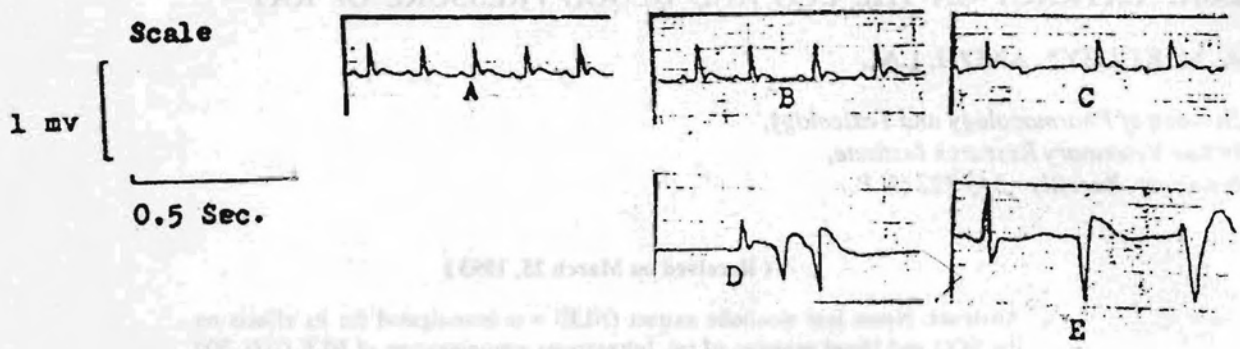

Fig. 1 : Effect of NLE on the ECG of anaesthetized rat.
A - Normal, ECG (heart rate 360/min),
B - 100 mg/kg (decrease in heart rate, 300/min),
C - 300 mg/kg (decrease in heart rate, missing of beats and increase in P-R interval),
D & E - 1000 mg/kg (absence of P-wave and ventricular extra systoles).

The increased P-R interval indicated impaired conduction through the Bundle of His and the absence of P-wave suggested either prevention of impulse generation at the S.A. node or its conduction over the atria by NLE. The bradycardia observed after the administration of NLE might also be due to slowing of generation or conduction of impulses in the heart and the missing of beats could be the sequel of functional conduction block. Extrasystoles with prolonged and inverted QRS complexes suggested the production of impulses from an ectopic ventricular focus and its slow spread through the ventricular muscle to the rest of the ventricle due to the action of NLE (6).

Effect of NLE on B.P.

The normal mean B.P. of rats ranged in between 80-95 mm of Hg. NLE (100, 300 and 1000 mg kg^{-1}, i.v.) produced dose - dependent fall in the mean blood pressure (Fig. 2). The fall in blood pressure was sharp within 10 seconds of injection and persisted for a long time. A similar type of hypotensive effect in cat with sodium nimbidinate obtained from neem oil was reported earlier (7). Pretreatment with atropine (1 mg kg^{-1}, i.v.) and mepyramine (3 mg kg^{-1}, i.v.) did not block the hypotensive effect of NLE. This rules out the involvement of muscarinic and histaminergic receptors in causation of fall in B.P.

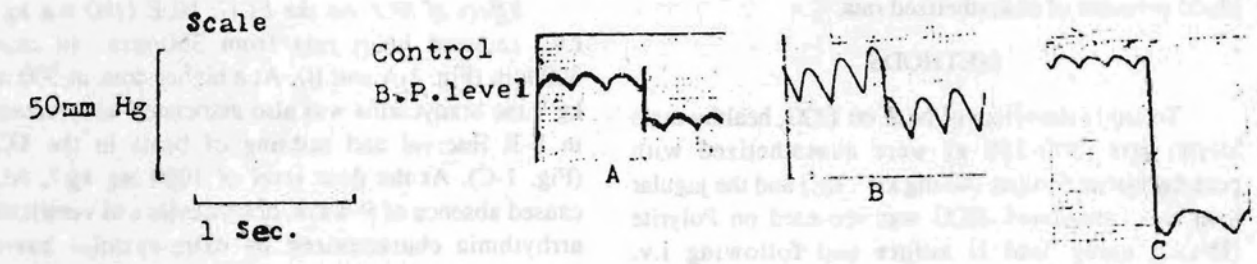

Fig. 2 : Effect of NLE on the blood pressure of anaesthetized rat.
A - NLE 100 mg/kg, B - NLE 300 mg/kg,
C - NLE 1000 mg/kg.

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