SOME PHARMACODYNAMIC EFFECTS OF PHENTHOATE

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ABSTRACT

Phenthoate (O, O-dimethyl S-alpha ethoxy carbonylbenzyl phosphorodithioate) was studied for its pharmacodynamic effects on blood pressure in dog, isolated frog heart, skeletal muscle (frog rectus abdominis) and smooth muscle (guinea pig ileum). Phenthoate did not produce consistent effect on blood pressure of dog. No effect on resting tone of skeletal and smooth muscle preparations was observed. Phenthoate neither inhibited nor potentiated the acetylcholine-induced contractions of skeletal muscles. However, it blocked non-specifically the acetylcholine, histamine, 5-hydroxytryptamine and barium chloride-induced contractions of guinea pig ileum. Phenthoate produced negative inotropic and chronotropic effect on isolated frog heart which was blocked by atropine, indicating the cholinomimetic effect as a result of cholinesterase inhibition which is the characteristic feature of organophosphorous compounds.

INTRODUCTION

Phenthoate (O, O-dimethyl S-alpha ethoxy carbonylbenzyl phosphorodithioate), an organophosphate, is a widely used insecticide and acaricide. Effects of phenthoate on various blood enzymes, haematological, biochemical and neuropharmacological parameters in mice, rats and buffalo calves have been reported (Punia et al., 1987; Punia et al., 1989a; Punia et al., 1989b; Punia et al., 1995). The reported effects were on the similar pattern as that of other cholinesterase inhibitors. However, information on the effect of this compound on various pharmacodynamic parameters in animals is lacking. Therefore, the present investigation was undertaken to evaluate the cholinomimetic effect of phenthoate on blood pressure, heart, skeletal and smooth muscles.

MATERIAL AND METHODS

Technical grade phenthoate (91%) was obtained from Bharat Pulverising Mills Limited, Bombay. It was suspended in 1% gum acacia in normal saline. Mongrel dogs of either sex weighing 6-10 kg were procured locally. Frogs (Rana tigrina) were obtained from Laboratory Animals Farm, Amritsar. Guinea pigs of either sex weighing 400-600 g were procured from Disease Free Small Animal House of CCS Haryana Agricultural University, Hisar. All the animals were maintained on standard feed and water ad libitum. The parameters studied were effect of phenthoate on blood pressure, isolated heart, skeletal and smooth muscles.

Effect of phenthoate on heart was investigated on isolated frog heart (n=5). The effect of graded doses of phenthoate (5, 10, 20, 40 and 80 mg/kg) were studied.

Effect of phenthoate on blood pressure was studied in four dogs anaesthetized with pentobarbitone sodium (30 mg/kg, i.v.) administered in saphenous vein. The femoral vein was cannulated and attached to a burette containing normal saline solution. The carotid artery was cannulated and connected with a tube filled with 10% sodium citrate as an anticoagulant and then connected to mercury manometer. The line of atmospheric pressure on kymograph was drawn according to the method of Duke (1955). The effect of graded doses of phenthoate viz., 5, 10, 20, 40 and 80 mg/kg were studied.

Effect of phenthoate on heart was investigated on isolated frog heart (n=5). The effect of graded doses of phenthoate and its effect on the response of heart to acetylcholine (ACh) and epinephrine was studied.

Isolated frog rectus abdominis muscle preparation (n=5, bath capacity: 30 ml) was used to study the effect of phenthoate on skeletal muscle. The effect of graded doses of
phenthoate and its effect on response of isolated muscle preparation to ACh was studied. ACh was added to the bath and allowed to act for 2 min. Phenthoate was allowed to act for 5 min. Between each addition of ACh or phenthoate, 4-5 washings were given to the tissue.

Effect of phenthoate on smooth muscle was studied using isolated guinea pig ileum (n=5, bath capacity: 30 ml). Segments of 2.5 cm of ileum were mounted in isolated organ bath as per standard procedure. The effect of graded doses of phenthoate and its effect on the response of tissue to ACh, histamine, 5-hydroxytryptamine (5-HT) and barium chloride (BaCl2) was studied.

RESULTS AND DISCUSSION

The graded doses of phenthoate viz., 5, 10, 20, 40, 80 mg/kg i.v. produced inconsistent effect on blood pressure. In some dogs, it produced no effect whereas, in others it produced a non-specific fall in blood pressure which was not even reproducible by the subsequent doses. It has been reported that most of the organophosphates caused marked fall in blood pressure (Salerno and Coon, 1949; Krop and Kunkel, 1954). A fall in systolic, diastolic, pulse and mean arterial pressure in anaesthetized dogs by Hinosan has also been reported (Malik, 1975).

Phenthoate in graded doses of 0.1, 1, 10, 100, 200 and 300 µg produced negative inotropic and chronotropic action on isolated frog heart (Fig. 1). It neither potentiated nor inhibited the action of ACh (0.01 µg) and epinephrine (0.1 µg) on heart. The negative inotropic and chronotropic effects of phenthoate were blocked by atropine (15 µg) indicating that phenthoate might be acting through cholinergic system.

Phenthoate in the concentration of 50 and 500 µg/bath did not cause any effect on the response of frog rectus abdominis muscle to ACh (6 µg/bath). In isolated tissues access is not usually a problem. However, Burgen et al. (1949) reported that DFP and HETP potentiated the ACh-induced contractions.

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Fig. 1. Effect of phenthoate on isolated frog heart.
Phenthoate at 50 and 500 µg/bath blocked the ACh (0.1 µg/bath), histamine (0.3 µg/bath), 5-HT (1.5 µg/bath) and BaCl₂ (2 mg/bath) induced contractions of guinea pig ileum, indicating a non-specific effect of phenthoate on the smooth muscles (Fig. 2). At lower concentration, it blocked the contractions up to 40-50 per cent whereas at higher concentration, it blocked the contractions to almost 100 per cent.

REFERENCES