CHANGES IN BRAIN ACETYLCHOLINE OF RATS AFTER DERMAL APPLICATION OF FENITROTHION (SUMITHION)

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Summary: Fenitrothion (Sumithion), an organophosphorous insecticide, was applied dermally to rats. Cholinesterase activity was measured in blood and brain. The concentration of the pesticide in blood plasma and acetylcholine in brain were estimated at different intervals. The maximum concentration of Fenitrothion in the plasma was found at 4 hrs while significantly elevated levels of acetylcholine were present in the brain till 24 hrs. The results suggest that the compound was readily absorbed by dermal route to produce inhibition of cholinesterase and a consequent persistent increase in brain acetylcholine.

Key words: organophosphorous compound, Fenitrothion, dermal, absorption, Acetylcholine (Ach), Cholinesterase (ChE)

INTRODUCTION

It is well established that organophosphorous compounds inhibit the cholinesterase activity and increase the level of acetylcholine (4). The accumulation of acetylcholine in the brain leads to excitatory effects like tremors and convulsions (6). In most of these studies only the level of compound or the cholinesterase activity was determined after administration of organophosphorous compounds.

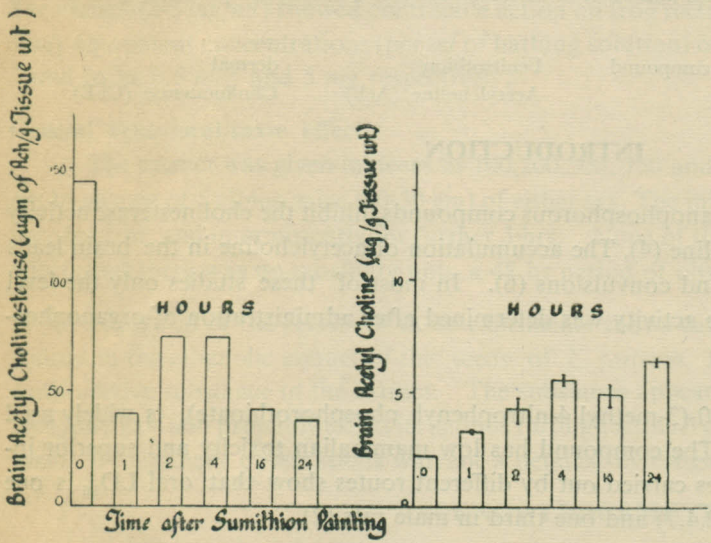
Fenitrothion, 0, 0-dimethyl 0-(3-methyl 4-nitrophenyl phosphorothioate), is widely used for control of agriculture pests. The compound has low mammalian toxicity and superior insecticidal activity. Toxicity studies carried out by different routes show that oral LD_{50} is one fourth of dermal LD_{50} in mouse (2,4,7) and one third in male rats (2).

An insecticide may gain entry into the system through any of the major portals, viz., oral, respiratory and dermal routes. Under normal conditions of manufacture, handling and spraying of insecticides large quantities of material come in contact with the skin of the workers and remain on the body surfaces for long periods. This may cause local skin lesions and systemic manifestations after getting absorbed into the system. Since the most likely route of entry is through the skin, it was considered worthwhile to assess the degree of absorption of fenitrothion from the skin and its effect on brain acetylcholine.

The present study was undertaken to determine the concentration of acetylcholine in brain, level of acetylcholinesterase activity in blood and brain as well as the level of fenitrothion in the plasma at different intervals after a single dermal application of the insecticide (750 *mg/kg*) in rats.

MATERIALS AND METHODS

Female albino rats of I.T.R.C. stock weighing 150-170 g were used in the present study. The skin over the back between the shoulders and hind quarters were shaven with an electric clipper. The rats were randomized into several groups of six rats each and placed in individual cages. Food and water were supplied *ad-libitum*. One group served as controls. The rats of the other groups were painted a single LD_{50} dose of 750 *mg/kg* of fenitrothion over an area of 2 x 2 cm and were sacrificed at intervals of 1, 2, 4, 16 and 24 hrs by decapitation method. Blood was collected in an oxalated tube. Brains were removed quickly. The brain acetylcholine was extracted by the method of Smallman and Fisher (5) and assayed by using guinea pig ileum. The concentration of fenitrothion in plasma was determined by spectrophotometric method (3), cholinesterase activity was assayed by the method of Hestrin (1).



(a) (b)

Fig. 1: Cholinesterase activity and level of acetylcholine in brain at different intervals after painting 750 *mg/kg* of fenitrothion on 2 x 2 cm of rat skin. The values are mean ±S.E. of the values of six animals.

RESULTS AND DISCUSSION

It is epitomized from the Fig. 1 a and b that there was an inhibition in enzyme activity of brain (ᔕ 75%) and an elevation in acetylcholine level at one hr after fenitrothion painting. The inhibition in enzyme activity lead to accumulation of acetylcholine in increasing order at 2, 4, 16 and 24 hrs. In contrast, there was a slight recovery in the enzyme activity at 2 and 4 hrs with a subsequent fall at 16 and 24 hrs. It could be possible that the enzyme tended to recover itself at 2 and 4 hrs from the inhibitory effect of the compound. It is proposed that the cholinesterase affects the hydrolysis of acetylcholine but its synthesis remains unaffected. A similar picture was obtained in the blood cholinesterase (Fig. 2).

Accroding to Stewart (6), the concentration of acetylcholine in the brain is directly related to the symptoms like tremors and convulsions. Tremors and convulsions appeared in the experimental animals also.

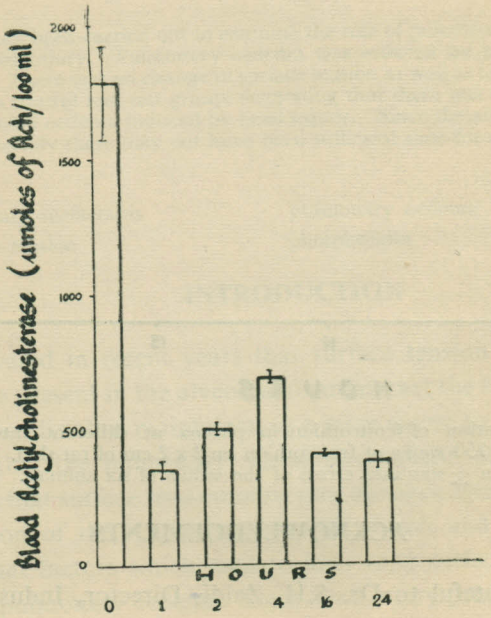


Fig. 2: Cholinesterase activity at different intervals in the blood of rats after painting 750 *mg/kg* of fenitrothion on 2 x 2 cm of rat skin. The values are mean ±S.E. of the values of six animals.

The estimation of fenitrothion in the plasma after dermal application of the compound (Fig. 3) showed that the compound was readily absorbed through the rat's skin and significant amounts of the compound were present at 1 hr after dermal application. The plasma level of fenitrothion increased with time and reached maximum at 4 hrs with a continuous decrease at 16 and 24 hrs, whereas the acetylcholine level increased continuously and was maximum at 24 hrs. It could be possible that the persistence of the parent compound or its metabolites across the blood brain barrier alter the dynamics of the acetylcholine.

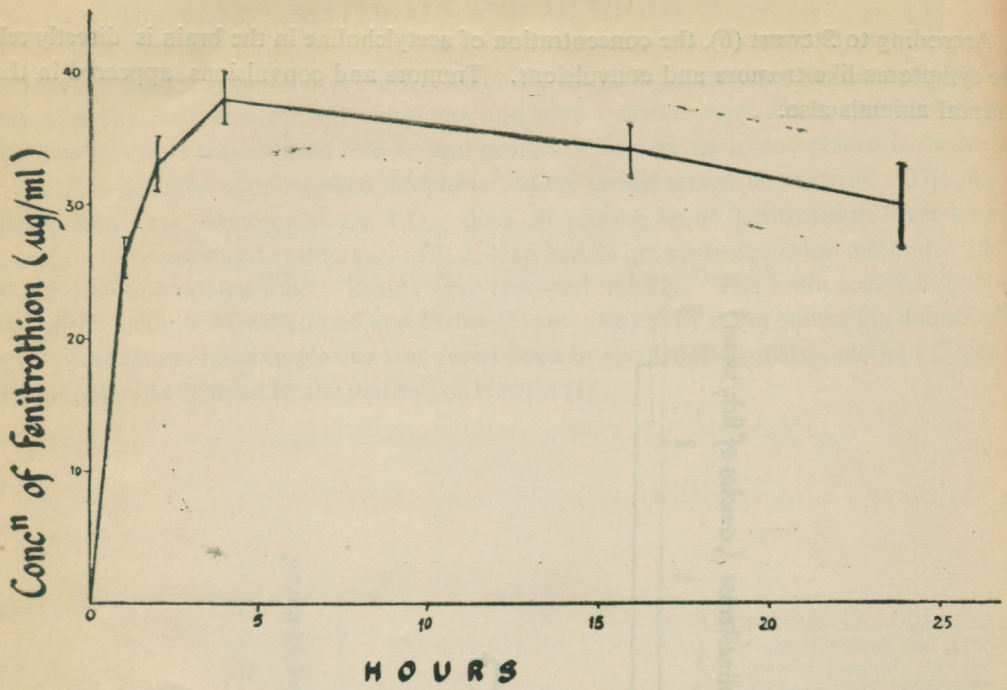


Fig. 3: Concentration of fenitrothion in plasma at different intervals after painting 750 *mg/kg* of fenitrothion on 2 x 2 cm of rat skin. The values are mean ± standard errors of the values of six animals.

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