Effect of Malathion on the Content of Fenitrothion and Fenitrooxone in the Rat

by A. HLADKÁ, V. KRAMPL, and J. KOVAC
Institute of Industrial Hygiene and Occupational Medicine
and
Research Institute of Agrochemical Technology
Bratislava, Czechoslovakia

The interactions of organophosphorus pesticides resulting in an increase of their toxicity are repeatedly discussed. Various investigators discuss this question mostly from the view of the inhibition of cholinesterase and other esterases /Murphy 1969, Moeller and Rider 1962/ or from the view of the potentiation of acute toxicities /Du Bois and Kinoshita 1963/.

In this paper the attention was paid to the changes of the content of two organophosphorus pesticides of low toxicity fenitrothion and malathion - and also to their toxic metabolites- oxones in the tissues of rats after the individual or simultaneous administration of these compounds. Such an approach to the study of this problem was facilitated by the use of multidetectional analytical method of high sensitivity.

Materials and Methods

Wistar female rats weighing 200 g were used in these experiments. Insecticides were administered in water emulsion with Tween 80 by means of oral tube. There were three experimental groups. Twoo groups received a single dose of 200 mg/kg b.w. of fenitrothion or malathion. The third group of animals received a

Address for reprints: Dr. A. Hladká, Bratislava, Dukelská 20, Czechoslovakia

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combination of fenitrothion with malathion in a single dose of 200 mg/kg and 200 mg/kg b.w., respectively.

The animals were sacrificed by decapitation in certain time intervals from 30 min to 24 hr after the administration of drugs. Each subgroup consisted of 4 rats. Both the fenitrothion and malathion used were of chromatographic purity. The authentic oxones were prepared by the oxidation of fenitrothion and malathion with peracetic acid by the method of Patchett and Batchelder /1960/. The purity of the prepared oxones was checked by chromatographic methods.

The level of unmetabolized insecticides and their corresponding oxones was estimated in the liver, muscle and in blood. These residues were isolated by the extraction with a solution of benzene and acetone /2:1/ from the column consisting of the mixture of Siloxid[1] and tissue homogenate in acetone and benzene /Hladká and Kováč 1973/. After a simple purification of extracts /Hladká and Kováč 1973/ the unmetabolized pesticides were estimated by technique of gas chromatography and oxones were semi-quantitatively determined by thin-layer chromatography.

The conditions of fenitrothion and malathion determination:Gas Chromatograph Fractovap D /Carlo Erba/ equipped with a parallel flame thermionic detector. Glass column /160 cm x 0.3 cm/packed with 5% OV 1 /w/w/ on Anakrom ABS 70/80 mesh. The temperature of the column was 195°C and that of detector was 210°C. Gas flows: carrier gas N_2 15 ml/min, H_2 45 ml/min and air 410 ml/min. Thiometon was used as internal standard. The yield of this method was 90.6 $\pm$ 8.2%, the minimal detectable quantity was 0.025 ng.

The oxones were estimated semiquantitatively

[1]Siloxid is precipitated active silicon dioxid /Tonaso, Neštěmice, Czechoslovakia/

by thin-layer chromatography on silica gel with the use of enzymatic detection/Ackermann et. al. 1969/. The average yield was 83%, the minimal detectable quantity was 0.5 ng of oxones.

Results and Discussion

The levels of fenitrothion on the liver, blood and muscle after the administration of fenitrothion and a combination of fenitrothion and malathion are presented in Fig. 1-3. The level of fenitrothion in the liver was decreased in the presence of malathion. In the blood and muscle an increase of fenitrothion was observed with a maximum at 12 hr after the administration which followed the initial decrease of this level. After 24 hr the differences in all groups of animals were not statistically significant.

An exponential decrease of fenitrooxone level /Fig.4-6/ after the administration of fenitrothion was found in all cases. After the administration of the mixture of fenitrothion and malathion a shift of the maximum level to the later time intervals was observed and simultaneously a statistically significant increase of fenitrooxone level occurred.

The increased levels of fenitrooxone after the administration of a combination of fenitrothion and malathion point out a prolonged persistance of oxidative metabolite in the tissues and this finding was mostly remarkable in muscles. However, in the experiments of Du Bois and Kinoshita /1963/ on the increase of acute toxicity of fenitrothion in a combination with malathion no sings of a potentiating affect were found.

Malathion was found in the tissues until the 30 st minute after its administration /Fig. 7/. The differences in the malathion level in the liver and muscles following the individual and combined administra-

Time changes of fenitrothion content after a single administration of fenitrothion in a dose of 200 mg/kg and a combination of fenitrothion and malathion 200 mg/kg and 200 mg/kg, respectively.

Fenitrothion ———————— ; fenitrothion and malathion ---------- ;

Significance levels: ● = P<0.05 - 0.001, 0 = N.S.

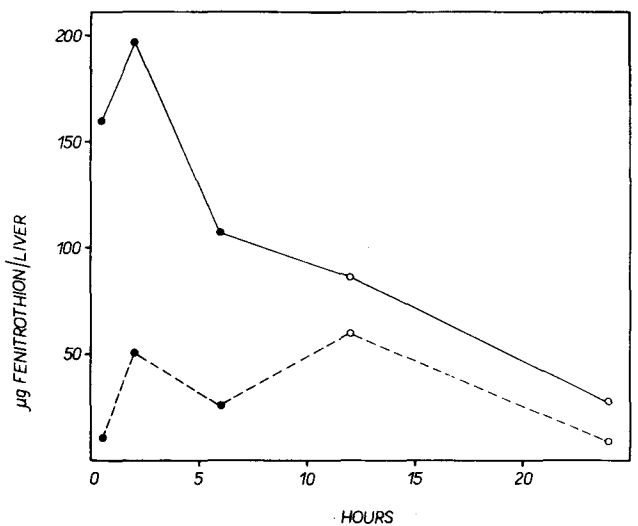

Fig. 1. Time changes of fenitrothion content in the liver.

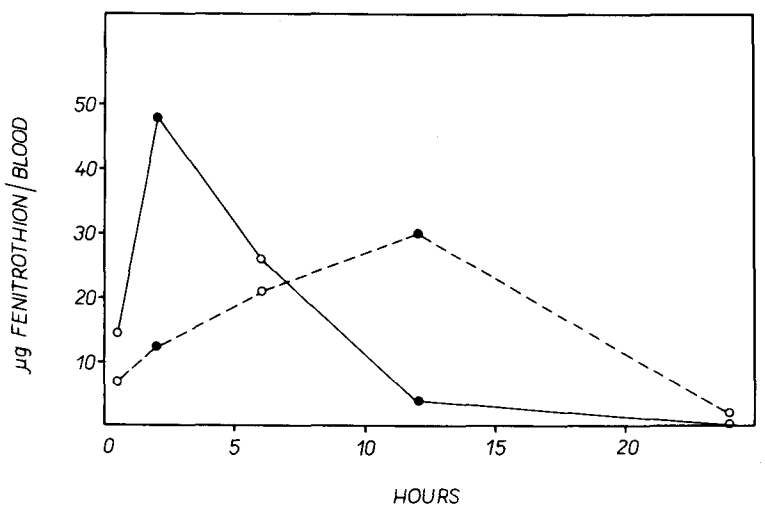

Fig. 2. Time changes of fenitrothion content in blood.

Time changes of fenitrothion and fenitrooxone content after a single administration of fenitrothion in a dose of 200 mg/kg and a combination of fenitrothion and malathion 200 mg/kg and 200 mg/kg, respectively.
Fenitrothion ———————— ; fenitrothion and malathion --------- ;
Significance levels: ● = P< 0.05 - 0.001, O = N.S.

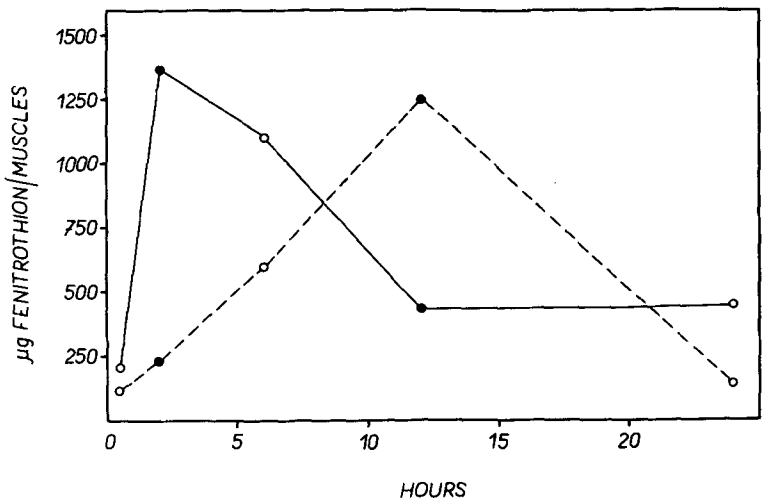

Fig. 3. Time changes of fenitrothion content in muscles.

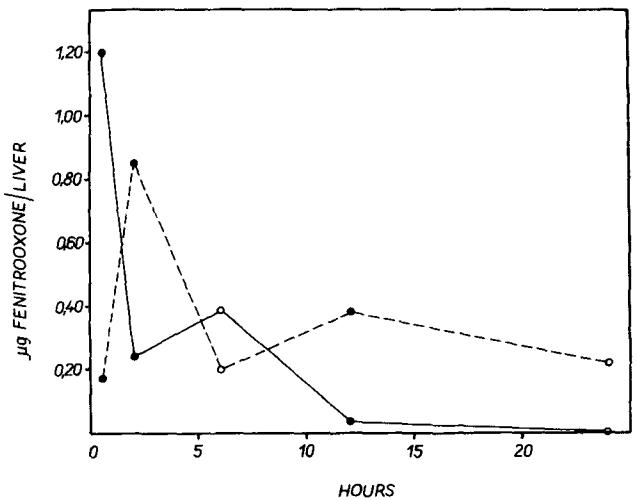

Fig. 4. Time changes of fenitrooxone content in liver.

Time changes of fenitrooxone content after a single administration of fenitrothion in a dose of 200 mg/kg and a combination of fenitrothion and malathion 200 mg/kg and 200 mg/kg, respectively.

Fenitrothion ———————— ; fenitrothion and malathion --------- ;

Significance levels ● = $P<0.05 - 0.001$, 0 = N.S.

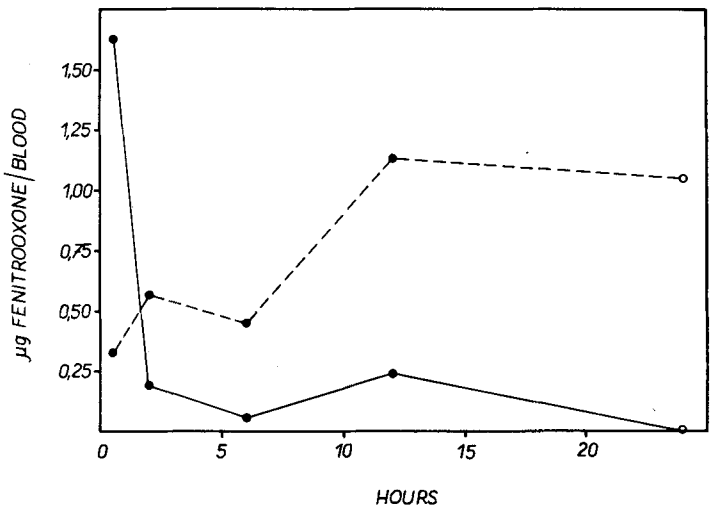

Fig. 5. Time changes of fenitrooxone content in blood.

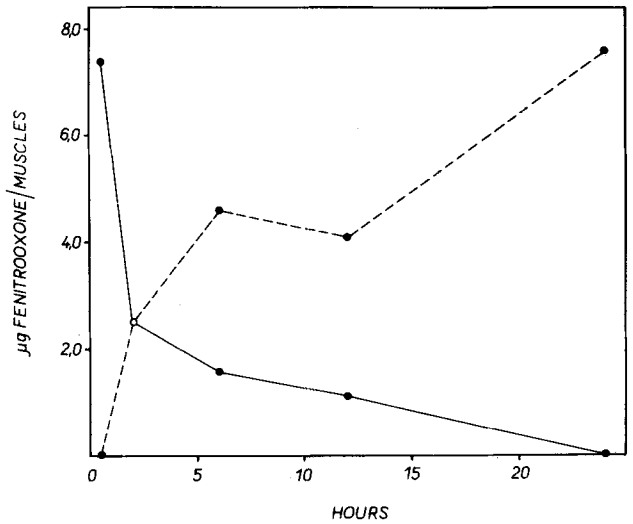

Fig. 6. Time changes of fenitrooxone content in muscles.

tion were statistically significant. In these samples no malaoxone was detected.

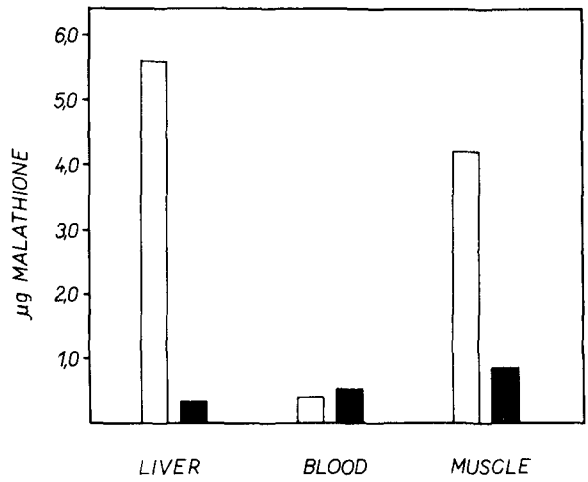

Fig. 7. The content of malathion in liver, blood and muscles of rats 30 min after the administration of 200 mg/kg malathion and of a combination of fenitrothion /200 mg/kg/ and malathion /200 mg/kg/.
Malathion □ ; malathion and fenitrothion ■ .

A rapid decrease of fenitrothion content is in accordance with data reported by Miyamoto et al. /1963, 1964/. Also the rapid destruction of malathion in water soluble metabolites and a low stability of malaoxone in mammalia /March et al. 1956, O'Brien 1957, Metcalf and March 1953/ are in correspondence to our data.

On the basis of these data it cannot be concludet that there is a potentiation of the toxicity of fenitrothion and malathion, although the increase of fenitrooxone levels in the tissues examined makes such and explanation possible.

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