## МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ ВИЩИЙ ДЕРЖАВНИЙ НАВЧАЛЬНИЙ ЗАКЛАД УКРАЇНИ «БУКОВИНСЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ»



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Загальна редакція: професор Бойчук Т.М., професор Іващук О.І., доцент Безрук В.В.

Наукові рецензенти: професор Братенко М.К. професор Булик Р.€. професор Гринчук Ф.В. професор Давиденко І.С. професор Дейнека С.Є. професор Денисенко О.І. професор Заморський I.I. професор Колоскова О.К. професор Коновчук В.М. професор Пенішкевич Я.І. професор Сидорчук Л.П. професор Слободян О.М. професор Ткачук С.С. професор Тодоріко Л.Д. професор Юзько О.М. професор Годованець О.І.

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## Korotun O.P.

## TOXICOLOGICAL ASSESSMENT OF INDIVIDUAL SUSCEPTIBILITY TO ACUTE POISONING BY ORGANOPHOSPHORUS PESTICIDES IN VIVO

Department of Hygiene and Ecology Higher State Educational Establishment of Ukraine "Bukovinian State Medical University"

Modern agriculture and greenhouses development often require intensive pesticide use, which raises serious concerns over food safety and human health. Besides, pesticide self-poisoning accounts for one-sixth to one-eighth of the world's suicides and a third of suicide deaths in rural Asia each year (Bajracharya S.R., 2016).

Organophosphorus pesticide (OP) self-poisoning is an important clinical problem in rural regions of the developing world and kills an estimated 200 000 people every year. Unintentional poisoning kills far fewer people but is a problem in places where highly toxic organophosphorus pesticides are available. Medical management is difficult, with case fatality generally more than 15% (Eddleston M., 2013).

OP pesticides inhibit cholinesterase enzymes leading to overstimulation of cholinergic receptors. Clinical features depend on the types of receptors stimulated at various sites of the body. Measurement of plasma cholinesterase is useful for the diagnosis of OP poisoning although it may not directly correlate with the severity of the poisoning. Consequently, individual features of enzymes activity influence the susceptibility of the organism to OP toxic effects. The higher susceptibility of "rapid acetilators" to subchronic intoxication we have proved in previous studies (Korotun O.P., Vlasyk L.I., 2014, 2018).

This study investigates individual susceptibility to acute OP (dimethoate) poisoning in the experimental model.

The experiment was done in 42 white male rats, using the authors' modification of the loading test with amidopyrine. N-acetyltransferase phenotype (as "rapid" and "slow" acetylation type) was determined based on the rate of 4-amino-antipyrine and N-acetyl-4-aminoanthypirine excretion with urine.

Acute intoxication was modeled by a single intragastric administration of dimethoate at a dose of 200 mg/kg. The DL50 was calculated by the van der Varden method.

All manipulations were carried out following the criteria outlined in the European Union Directive 2010/63/EU "On the protection of animals used for scientific purposes" (2010). All data are represented as a mean  $\pm$  standard error of the mean (M $\pm$ m). The minimum significance level was p<0.05.

The DL50 of the dimethoate and the average time of death of the "slow" acetylators ( $230.0 \pm 26.00$  mg/kg and  $40.0 \pm 4.50$  hours correspondently) were not significantly different from those of animals with the "rapid" acetylation type ( $190.0 \pm 15.50$  mg/kg and  $34.0 \pm 5.50$  hours).

However, the number of animals that survived the 200 mg/kg dose was significantly greater among the "slow" acetylators and included 75% (vise 42% surviving among the "rapid" acetylators).

Thus, animals with different acetylation phenotypes have different susceptibility to the adverse effects of Organophosphorus pesticides.

Assessment of acetylation activity level could be used as an inexpensive, non-invasive and relevant index of organism susceptibility to OP. The risk of acute poisoning development, in a genetically susceptible population group, should be estimated using susceptibility biomarkers and include phenotype research to reach proper validation and qualification.