

Toxicity of insecticide mixture is sum of its parts, a cell study finds.

Aug 10, 2011

Cao, Z, TJ Shafer, KM Crofton, C Gennings and TF Murray. 2011. **Additivity of pyrethroid actions on sodium influx in cerebrocortical neurons in primary culture.** Environmental Health Perspectives <http://dx.doi.org/10.1289/ehp.1003394>.

Synopsis by Tamara Tal

Widely used pyrethroid insecticides that share a common nerve cell target produce a larger toxic effect than each chemical on its own, according to a rodent brain cell study that verifies prior animal studies.

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A mixture of almost a dozen, similar-acting insecticides that are used on food crops can act in concert to produce effects in mouse brain cells on par with the sum of each chemical's individual effect, reports a team of academic and government researchers. Together, the 11 pyrethroid insecticides – tested at levels that mimic real-world exposures – over-stimulate electronic channels in the cells, an action that eventually kills them.

This study is important because it shows for the first time that common insecticides converge on the same cell target to produce heightened toxicity. Scientists call this type of increased toxicity “additive” because the mixture produces a toxic response that is equal to the sum of each individual effect.

Pyrethroids are synthetic insecticides found in more than 3,500 registered products, many of which are used in homes, on pets and in agriculture. These insecticides are designed to mimic the effects of the natural toxins found in chrysanthemum flowers.

Pyrethroid insecticides are toxic to insect pests and humans in the same way. They target vital electrical channels – called voltage-gated sodium channels – in certain types of brain cells known as neurons. The chemicals essentially boost the electrical signals that are moving into the cells. The over-activation of these channels changes neuron function and ultimately leads to paralysis and death in the targeted pest.

Researchers at Creighton University and the U.S. Environmental Protection Agency collected mice brain cells and exposed them to the pyrethroids singly or in a mixture. They wanted to test whether the combined effect of multiple pyrethroids is equal to the sum of their individual effects. They used nerve cells from mice to understand what might happen in humans.

The researchers found differences in each chemical’s ability to affect the cellular channels. Seven triggered a strong effect, two pyrethroids produced a mild response, and two had no effect. A known inhibitor blocked the actions of the active pyrethroids. Together, these confirm that the active chemicals have the same target.

When the researchers exposed neurons to all 11 compounds simultaneously, they found that the combined effect of the mixture was equal to the sum of the effects of the individual pyrethroids.

This study is important because it confirms the prevailing assumption that pyrethroid mixtures produce additive toxicity by converging on electrical channels in brain cells.

The pyrethroid compounds tested – deltamethrin, β -cyfluthrin, cypermethrin, permethrin, bifenthrin, esfenvalerate, λ -cyhalothrin, tefluthrin, fenpropathrin, resmethrin and S-bioallethrin – are mainly used to control pests on food crops.



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8 July **Cumulative Effects of dibutyl phthalate and diethylhexyl phthalate on Male Rat Reproductive Tract Development: Altered Fetal Steroid Hormones and Genes -- Howdeshell et al., 10.1093/toxsci/kfm069 -- Toxicological Sciences** Exposure to a mixture of phthalates causes reproductive harm in an additive manner. Toxicological Sciences.

1 July **Dysgenesis and Histological Changes of Genitals and Perturbations of Gene Expression in Male Rats after In Utero Exposure to Antiandrogen Mixtures -- Metzdorff et al. 98 (1): 87 -- Toxicological Sciences** Prenatal exposure to a mixture of anti-androgenic chemicals produces changes in the structure of and genes expressed in male reproductive organs. Toxicological Sciences.

15 April **Sequelae in male rabbits following developmental exposure to p,p'-ddt or a mixture of p,p'-ddt and vinclozolin: cryptorchidism, germ cell atypia, and sexual dysfunction** Exposure to a mixture of anti-androgenic chemicals during development leads to male reproductive abnormalities. Food and Chemical Toxicology.

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6 April **Neurotoxicological and statistical analyses of a mixture of five organophosphorus** Science Byte: A mixture of 5 organophosphates typical of human exposures causes synergistic impacts on behavior and brain neurochemistry in rats.

29 March **Protecting children from environmental toxins.** The consequences of exposure to many other chemicals or mixtures of chemicals, such as insecticides—chemicals oftentimes specifically designed to be toxic—are largely unknown. PLOS Medicine.

2 May **A Mixture of Dioxins, Furans, and Non-ortho PCBs Based upon Consensus Toxic Equivalency Factors Produces Dioxin-Like Reproductive Effects -- Hamm et al. 74 (1): 182 -- Toxicological Sciences** Exposure to a mixture of PCBs, dioxins and furans is found to have effects similar to TCDD. Toxicological Sciences.

17 September **Herbicides reduce fetal implantation rates.** Wisconsin researchers show a commercial mixture of lawn chemical herbicides to cause fetal loss in mice. ProtectingOurHealth.org.

1 September **Xenoestrogens at levels below Individual No-observed-effect Concentration Dramatically Enhance Steroid Hormone Action** The combined impact of even a small number of estrogen-like compounds in a mixture can be very significant. OurStolenFuture.org.

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