Developmental disorders induced by pesticide degradetion products

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Summary

Deducing the potential risks of pesticides by considering the parent compounds alone is inadequate, because pesticides do transform in the environment after application. This thesis addressed the adverse effects of pesticides arising from their environmentally stable breakdown products and explored the probable long-term effects of these degradation products in comparison to those arising from the parent compounds.

Based on the massive usage of pesticides and potential for increased pesticide use in its catchment, the river Nzoia (Kenya) was studied for contamination with chloroacetanilides and their stable aniline degradation products (Chapter 2). Alachlor, metolachlor and their respective environmentally stable aniline degradation products, 2,6-diethylaniline and 2-ethyl-6-methylaniline were analyzed in water and sediment samples from 9 sites along the river, using gas chromatography. These tests revealed a comparatively higher concentration and frequency of detection of the degradation products than the parent compounds in both sediment and water samples. A widespread occurrence of the degradation products during the study period indicated their persistence in the environment. It was concluded that the prevailing tropical climatic conditions favor a quick break down of the pesticides into their environmentally stable degradation products, thereby making the latter more important pollutants than their parent products in the study area. The toxic risk of these degradation products were therefore investigated in the succeeding research steps (Chapters 3-5).

It is generally believed that degradation products of pesticides are less toxic than their parent compounds. This belief is, however, invariably based on the acute lethal effects. Long term risks and other toxicity endpoints are seldom considered. Therefore in Chapter 3 the relative toxicological properties of the degradation products were investigated in different biological systems. Toxic and genotoxic effects of alachlor, metolachlor, amitraz, chlordimeform, their respective environmentally stable degradation products 2,6-diethylaniline, 2-ethyl-6-methylaniline, 2,4-dimethylaniline, and two other related compounds, 3,4-dichloroaniline and aniline were compared. Acute toxicity tests with *C. riparius* (96 h) and *V. fischeri* (Microtox®) and genotoxicity tests with a dark mutant of *V. fischeri* (Mutatox®) were carried out. Our results demonstrated that toxicity and

genotoxicity of the pesticides are retained upon degradation into their alkyl-aniline metabolites. In the case of the herbicides alachlor and metolachlor, the toxicity to *V. fischeri* was enhanced upon degradation. Narcosis alone explained the toxicity of the compounds to the midge, but not so for the bacteria, suggesting a disparity in the selectivity of the test systems. All compounds showed direct genotoxicity in the *Vibrio* test, but amitraz and its metabolite were genotoxic at concentrations 10^3-10^5 lower than all the other compounds. These observations indicate that stable degradation products of pesticides may contribute considerably to the environmental risks of pesticide application and that genotoxic effects may arise upon degradation of pesticides.

The fact that the pesticides studied here, chloroacetanilide and formamidine degradation products, were found to be genotoxic (Chapter 3) raised the question on the possible implications for developing embryos. During the embryonic development the living organism undergoes several gene-guided, cellular and molecular processes to generate a complex multicellular organism from a zygote making the embryos the 'weak link' in a life cycle of an organism. A substantive gene alteration will lead to death of the embryo, while a benign change may be carried on in life leading to developmental disorders, cancers, mutations or loss of fertility. Embryos at midblastula to early gastrula stages of a locally abundant African clawed frog *Xenopus laevis* were used as test organisms (Chapter 4 and 5). The embryos were exposed to the test chemicals for 96h. The lethal toxicity, growth and teratogenic effects of the compounds were investigated. An embryonic teratogenic index (TI; which is expressed as 96h-LC50/96h-EC50(malformation)) allows comparison of teratogenic risks of diverse compounds and mixtures. The teratogenicity of highly embryolethal compounds would obviously be less relevant in the environment compared to that of less lethal compounds, which have a potential to cause malformation in a large number of surviving organisms (Chapter 4-5). In addition paraquat was tested (Chapter 5). Like the formamidines and the chloracetanilides, paraquat is a chlorinated hydrocarbon. It is mainly photo-chemically degraded on the plants by the ultraviolet light from the sun into 4-carboxy-1-methylpyridinium chloride and methylamine hydrochloride as the major decomposition products.

The parent chloroacetanilides and formamidine were more acutely toxic than their stable aniline degradation products, however, the latter

proved more teratogenic (Chapter 4). The most common teratogenic effects of the parent compounds were edema as opposed to axial flexures and eye abnormalities for 2,6-diethylaniline and 2-ethyl-6-methylaniline and depigmentation with encephalomegaly for 2,4-dimethylaniline. The edema is a symptom of osmoregulatory disruption resulting from cell membrane disruption while the aberrations caused by the degradation products are diverse. Therefore, the chloroacetanilides and the formamidines are potential sources of teratogenic transformation products. Paraquat was found to cause growth retardation and flexures of the notochord similar to earlier observations in the larger embryos of *Rana pipiens*.

In the concluding remarks (Chapter 6) an overview of the chain of effects from pesticide application to adverse environmental effects is given. The implication of the present results for the environment and in regulatory practices of the pesticides in Kenya is addressed. After application pesticides degrade through several intermediary stages to the environmentally stable degradation products. Environmental conditions in the tropics favor quick breakdown of the pesticides, but the resultant transformation products, which are persistent and more water-soluble, dissipate more easily from the point of application to other environmental compartments. Even though the acute lethal toxicity of the pesticides is attenuated upon degradation, the resulting transformation compounds present new types of risks, as was revealed in a battery of 4 test systems in this study. The transformation products retained genotoxicity, while teratogenicity was enhanced compared to their corresponding parent compounds. Hitherto, the toxicity of the degradation products of commonly used pesticides has been ignored. My findings underline the need to identify, quantify and study pesticide degradation products in order to incorporate them in pesticide admission and regulatory processes.