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# Stereoselective Metabolism of 1,2,4-Triazole Fungicides in Hepatic Microsomes and Implications for Risk Assessment

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The 1,2,4-triazole fungicides (i.e., conazoles) are potent cytochrome P450 (CYP) modulators and have been used extensively in agriculture and medicine. Recently, emphasis has been placed on the potential adverse effects of these compounds on mammalian steroid biosynthesis and endocrine system disruption; some conazoles have also been linked to tumor formation in rodents. Although nearly all the conazole fungicides are chiral, and in some cases formulated as specific mixtures of diastereomers, relatively little is known about the environmental fate, metabolism and toxicity of individual diastereomers and enantiomers. We have utilized in vitro metabolism assays in conjunction with enzyme inhibitors, human CYPs, and molecular modeling to elucidate the mechanisms and kinetics of stereoselective and stereospecific conazole metabolism in vertebrate and invertebrate species, including humans. Results will be presented that illustrate the use of these techniques for studying xenobiotic transformations in biological systems and how experimental results are used to improve risk assessment.