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Sex- and species-dependent difference of methoxychlor *O*-demethylation by rat and mouse liver microsomes

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Abstract:

The *in vitro* metabolism of methoxychlor (MXC) and its mono-demethylated metabolites (mono-OH-MXC, including (*R*)- and (*S*)-enantiomers), was investigated using liver microsomes from rats and mice to rationalize the sex-dependent difference of MXC metabolism in rats. Kinetic analyses based on Eadie–Hofstee plots suggested that multiple enzymes were involved in MXC *O*-demethylation, whereas *O*-demethylation of mono-OH-MXC followed a standard one-enzyme model in all animal species studied. The kinetic parameters (V_{\max} , K_m) indicated that enhanced enzymatic efficiency (CL_{int}) in male rats was the cause of the sex-dependent metabolism of MXC in rats, while no such marked sex difference was observed in mice. It further appeared that female rats showed great enantioselectivity in *O*-demethylation that seemed to also be responsible for the sex-dependent metabolism. © Pesticide Science Society of Japan

Keywords:

sex difference, species difference, enantioselective metabolism, cytochrome P450, estrogenic responses, metabolic activation

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