Alterations in mouse liver monooxygenases by benzothiadiazoles

Pedemonte, Jaime

Olate, Juan

Cervantes, Paulina

Oberti, Carlos

Gil, Lionel

Administration of 1,2,3-benzothiadiazoles to mice had a biphasic effect on liver microsomal monooxygenases. During the first 15 hr of treatment, an inhibition of the in vivo metabolism of hexobarbital, as well as of the in vitro hydroxylation of naphthalene and N-demethylation of aminopyrine, was observed. An apparent decrease in cytochrome P-450 and in the activity of the NADPH-cytochrome c reductase also occurred. The levels of cytochrome b5 and NADH-cytochrome c reductase activity were only slightly affected. A shift to 452 nm in the carbon monoxide difference spectrum was obtained with dithionite-reduced microsomes and this was not modified by ferricyanide. After the initial inhibitory phase, an enhancement of drug-metabolizing activities in vivo and in vitro and in the levels of some components of the mixed function oxidase system was observed. The carbon monoxide difference spectra of dithionite-reduced microsomes returned to a maximal absorption at 450 nm. The stimulatory effect