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zool@tubitak.gov.tr

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Characterization and Structure-Function Studies of Human Liver Flavin Monooxygenase Isozyme 3 (FMO3)

Orhan ADALI
Middle East Technical University, Dept. of Biology, 06531 Ankara-TURKEY
Richard M. PHILPOT
National Institute of Environmental Health Sciences, National Institute of Health, Research Triange Park, 27709 NC-USA

Abstract: The activity of the flaving-containing monooxygenase (FMO EC 1.14.13.8) can be modulated by a number of nitrogen-containing compounds in a manner that is both isoform and effector-dependent. We showed that the direction (activation or inbihiton) and extent of modulation can also be dependent on substrate concentration. The native human liver FMO3 and arg 433 mutant FMO3 catalyze the methimazole reaction with similar Km values. However, the mutant FMO3-catalyzed reaction was affected differently by high concentration of imipramine, imipramine causing inhibition of activity. Our results suggest that the response of FMO3 to imipramine involves a distribution of compounds between two sites which is regulated by structural features.

Key Words: Flavin Monooxygenases (FMOs), Human, FMO3 isozyme, Imipramine, liver.

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