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Different Regulation of MROD Enzymatic Activity at a Basal Level and at Induced State with B[A]P: The Role of Adrenergic Receptors

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This study was designed to investigate the effect of central and peripheral adrenergic receptors on the regulation of methoxyesorufin 7-dealkylase (MROD) enzymatic activity, which is preferentially catalyzed by cytochrome CYPIA2. This cytochrome is involved in the metabolism of several drugs and other xenobiotics. MROD was determined fluorometrically in liver microsomes of adult male rats. Assessment took place at a basal level and at an induced state with B[a]P. Reserpine was used for central and peripheral catecholamine depletion and guanethidine for peripheral sympathectomy. In addition, a variety of adrenergic agonists and antagonists were used in order to test the hypothesis that adrenergic receptors are involved in the regulation of CYP1A2 (phenylephrine: α1-agonist; prazocin: α1-antagonist; dexmedetomidine: α2-agonist; atipamezole: α2-antagonist; isoprenaline: β1/β2-agonist and propranolol: β1/β2-antagonist). The data revealed the followings: a) The central nervous system (CNS) does not seem to affect basal MROD activity, while the sympathetic nervous system (SNS) seems to play a central role; b) peripheral α1-adrenoreceptors appear to be involved in the basal regulation of cytochrome CYP1A2, since when these receptors were blocked with prazocin, MROD activity decreased, while c) stimulation of the hepatic cell membrane β2-adrenoreceptors with isoprenaline increased MROD; d) on the other hand, the CNS plays a key role in the regulation of MROD inducibility with B[α]P. It seems that the CNS has a suppressive effect. In contrast, the SNS plays a stimulatory role in the regulation of this induction; e) central α2-adrenoreceptors are likely involved in the regulation of MROD inducibility with B[α]P, while f) blocking of α1-adrenoreceptors with prazocin strengthens the induction. In conclusion, peripheral adrenoreceptors play a significant role in the regulation of CYP1A2 at a basal level, whereas the induction of this enzyme with B[α]P is affected mainly by central adrenoreceptor.