Monoamine oxidase inhibitory properties of some methoxylated and alkylthio amphetamine derivatives. Structure-activity relationships

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The monoamine oxidase (MAO) inhibitory properties of a series of amphetamine derivatives with different substituents at or around the para position of the aromatic ring were evaluated. In in vitro studies in which a crude rat brain mitochondrial suspension was used as the source of MAO, several compounds showed a strong (IC50 in the submicromolar range), selective, reversible, time-independent, and concentration-related inhibition of MAO-A. After i.p. injection, the compounds induced an increase of serotonin and a decrease of 5-hydroxyindoleacetic acid in the raphe nuclei and hippocampus, confirming the in vitro results. The analysis of structure-activity relationships indicates that: molecules with amphetamine-like structure and different substitutions on the aromatic ring are potentially MAO-A inhibitors; substituents at different positions of the aromatic ring modify the potency but have little influence on the selectivity; substituents at the para position such as amino, alkoxyl, h