Structure-affinity relationships of halogenated predicentrine and glaucine derivatives at D1 and D2 dopaminergic receptors: Halogenation and D1 receptor selectivity

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Halogenation of the aporphine alkaloid boldine at the 3-position leads to increased affinity for rat brain D1-like dopaminergic receptors with some selectivity over D2-like receptors. A series of 3-halogenated and 3,8-dihalogenated (halogen = Cl, Br or I) derivatives of predicentrine (9-O-methylboldine) and glaucine (2,9-di-O-methylboldine) were prepared and assayed for binding at D1 and D2 sites. Halogenation of predicentrine led to strong increases in affinity for D1-like receptors, while the affinities for D2-like receptors were either practically unchanged or reduced three- to fourfold. Halogenated glaucine derivatives did not show any clear trend towards enhanced selectivity, and the affinities were poor and similar to or worse than the values previously recorded for glaucine itself. Together with earlier work on boldine derivatives, these results suggest that the 2-hydroxy group on the aporphine skeleton may determine a binding mode favoring D1-like over D2-like receptors, with e