Activity of cytisine and its brominated isosteres on recombinant human ?7, ?4?2 and ?4?4 nicotinic acetylcholine receptors

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Effects of cytisine (cy), 3-bromocytisine (3-Br-cy), 5-bromocytisine (5-Br-cy) and 3,5-dibromocytisine (3,5-diBr-cy) on human (h) ?7-, ?4?2- and ?4?4 nicotinic acetylcholine (nACh) receptors, expressed in Xenopus oocytes and cell lines, have been investigated. Cy and its bromo-isosteres fully inhibited binding of both [?-125l]bungarotoxin ([?-125l]BgTx) to h?7- and [3H]cy to h?4?2- or h?4?4-nACh receptors. 3-Br-cy was the most potent inhibitor of both [?-125l]BgTx and [3H]cy binding. Cy was less potent than 3-Br-cy, but 5-Br-cy and 3,5-diBr-cy were the least potent inhibitors. Cy and 3-Br-cy were potent full agonists at h?7-nACh receptors but behaved as partial agonists at h?4?2- and h?4?4-nACh receptors. 5-Br-cy and 3,5-diBr-cy had low potency and were partial agonists at h?7- and h?4?4-nACh receptors, but they elicited no responses on h?4?2-nACh receptors. Cy and 3-Br-cy produced dual dose-response curves (DRC) at both h?4?2- and h?4?4-nACh receptors, but ACh produced dual DRC only a