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Antagonistic properties of new non-phosphorylated derivatives of nitrogen-containing heterocycles towards P2 receptors

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Abstract

© 2015 Asisn Network for Scientific Informantion. P2 receptors are widely distributed in animal and human organisms; however, selective antagonists of these receptors are still lacking. One of the well-known and mostly used P2 receptor antagonist at present is pyridoxal-phosphate 6-azophenil 2', 4'-disulphonic acid (PPDAS) which has no selectivity to either P2X or P2Y receptors. In this study, a series of new PPADS analogues for their potential antagonistic effects on P2 receptors was tested. The compounds (lab codes 2a-2g) were tested at a concentration of 10 mM in vitro for antagonistic activity towards P2X and P2Y receptors using isolated rat smooth muscle preparations of urinary bladder, vas deferens and duodenum. Contractions of urinary bladder and vas deferens preparations were evoked by either agonist of P2X-receptors, a, (3-m ethyl ene-AT P (0.1-3 mM), or by electrical field stimulation (EFS, 0.5 msec, 100 V, 1-32 Hz) in the presence of M-cholinoblocker atropine (10 μM) and alpha-adrenoblocker phentolamine (10 μM). Relaxant responses of carbachol-precontracted duodenum preparations were induced by either ATP (1 μM-1 mM) or by EFS (0.5 msec, 100 V) with frequencies of 0.5, 1, 2 and 4 Hz. Effects of tested compounds were compared with that of PPADS (10 μM). It was found thatthe majority of the tested compounds showed some degree of antagonism against EFS-evoked contractions of rat isolated urinary bladder and vas deferens mediated via P2X receptors, however only compound 2c produced antagonism comparable with that of parent antagonist, PPADS. Further, compound 2c, unlike PPADS, did not antagonize P2Y-receptor-mediated relaxation in rat isolated duodenum preparations. It is concluded from this study that compound 2c is an effective antagonists of P2X but not P2Y receptors and it's selectivity towards subtypes of P2 receptors needs to be proved in further experiments.

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Keywords

Antagonists, Azophenylsulfonic acids, P2-receptors, Pyridoxine derivatives