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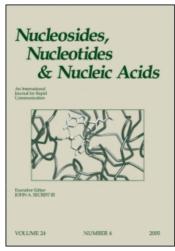
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Deaza-analogues of Adenosine and 2-Chloroadenosine as Agonists of Adenosine Receptors

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DEAZA-ANALOGUES OF ADENOSINE AND 2-CHLOROADENOSINE AS AGONISTS OF ADENOSINE RECEPTORS

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A variety of adenosine analogues have been recently evaluated in order to find more potent and selective agonists on adenosine receptors. The most potent adenosine analogues acting on A_1 receptor, a high affinity receptor inhibitory to adenylate cyclase, are N^6 -substituted compounds. So N^6 -cyclohexyladenosine (CHA) and N^6 -L-phenylisopropyladenosine (L-PIA) are extremely potent agonists on A_1 receptor, whereas they are relatively weak agonists on A_2 receptor, a lower affinity receptor which is stimulatory to cyclase, and they have no effect on the adenosine P site.

Recently we found that in a series of adenosine deaza-analogues the 1-deazaadenosine showed the highest affinity for adenosine receptors. We therefore have synthesized some N 6 -substituted 1-deaza-analogues of adenosine and 2-chloroadenosine and measured the IC $_{50}$ on $[^3H]N^6$ -cyclohexyl-adenosine (3H -CHA) and $[^3H]$ adenosine 5'-ethylcarboxamide (3H -NECA) binding selective for Λ_1 and Λ_2 receptors respectively. Binding assays were performed utilizing rat brain membranes. From the data obtained it was observed that also in the case of 1-deazaadenosine a cyclohexyl or a L-phenylisopropyl moiety at the N 6 position increases both the affinity and the specificity for Λ_1 receptor. The N 6 -L-phenylisopropyl-1-deazaadenosine showed the highest affinity for Λ_1 receptor in the series of 1-deaza-analogues so far examined, being three times less active than L-PIA. A chlorine atom at c^2 position increases binding affinity for Λ_1 receptor only in those analogues that are not substituted with other groups.