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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<sub>1</sub> receptor, a high affinity receptor inhibitory to adenylate cyclase, are N<sup>6</sup>-substituted compounds. So N<sup>6</sup>-cyclohexyladenosine (CHA) and N<sup>6</sup>-L-phenylisopropyladenosine (L-PIA) are extremely potent agonists on A<sub>1</sub> receptor, whereas they are relatively weak agonists on A<sub>2</sub> 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<sup>6</sup>-substituted 1-deaza-analogues of adenosine and 2-chloroadenosine and measured the IC<sub>50</sub> on [<sup>3</sup>H]N<sup>6</sup>-cyclohexyladenosine (<sup>3</sup>H-CHA) and [<sup>3</sup>H]adenosine 5'-ethylcarboxamide (<sup>3</sup>H-NECA) binding selective for A<sub>1</sub> and A<sub>2</sub> 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<sup>6</sup> position increases both the affinity and the specificity for A<sub>1</sub> receptor. The N<sup>6</sup>-L-phenylisopropyl-1-deazaadenosine showed the highest affinity for A<sub>1</sub> receptor in the series of 1-deaza-analogues so far examined, being three times less active than L-PIA. A chlorine atom at C<sup>2</sup> position increases binding affinity for A<sub>1</sub> receptor only in those analogues that are not substituted with other groups.