

## Selective inhibitory effect of adenosine A<sub>1</sub> receptor agonists on the proliferation of human tumor cell lines

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### Abstract

**Background:** In this study, the effects of three structural analogues of adenosine upon proliferation of human tumor cells were investigated. Previous research showed a cytotoxic effect of adenosine via A<sub>1</sub> receptor and A<sub>2</sub> receptor and sometimes this effect was receptor independent. The researches showed a differential cytotoxic effect of adenosine and its A<sub>1</sub> agonists on cancerous cells, while other studies demonstrated tumor promoting effect of adenosine and its A<sub>2</sub> agonists. The purpose of the present study was the evaluation of the possible selective anti-tumor effect of A<sub>1</sub> receptor agonists on cancerous cells. **Methods:** The substances of N<sup>1</sup>-cyclohexyl-adenosine (CHA, A<sub>1</sub> agonist), R-isomer of N<sup>1</sup>-phenylisopropyladenosine (R-PIA, A<sub>1</sub> agonist) and N<sup>6</sup>-ethylcarboxamido-adenosine (NECA, adenosine A<sub>1</sub>-A<sub>2</sub> non-specific agonist) were tested for their anti-proliferative effect using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay method. Hep G<sub>2</sub>, Hep<sub>2</sub>, CACO<sub>2</sub>, ACHN and L<sub>929</sub> cell lines were used in this assay. **Results:** CHA inhibited cell proliferation in three cell lines (in concentration of 0.01 μM) and R-isomer of R-PIA in one cell line (in concentration of 1.00 μM). These effects were inhibited partially by addition of 1,3-Dipropyl-8-cyclopentylxanthine (A<sub>1</sub> antagonist). The NECA analogue had no inhibitory effect on the cell proliferations. All of the substances had no cytotoxic effect on L<sub>929</sub> cells (mouse connective tissue fibroblast cell line). **Conclusion:** CHA and R-PIA had inhibitory effect on the proliferation of human tumor cell lines partially via A<sub>1</sub> receptor, while they didn't show such effect on fibroblast cells. These results suggest that A<sub>1</sub> adenosine receptor agonists have a good potential of specific anti-tumor activity.

### Reaxys Database Information

### Author keywords

A<sub>1</sub> receptor; Adenosine; Anti-tumor effect; Cytotoxicity; N<sup>1</sup>-cyclohexyl-adenosine (CHA); N<sup>1</sup>-phenylisopropyladenosine (R-PIA)

### Indexed Keywords

**EMTREE drug terms:** 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyltetrazolium bromide; 8-cyclopentyl-1,3-dipropylxanthine; adenosine 6'-N-ethylcarboxamide; adenosine A<sub>1</sub> receptor agonist; cyclohexyladenosine; dimethyl sulfoxide; phenylisopropyladenosine

**EMTREE medical terms:** animal cell; antineoplastic activity; article; cell proliferation; cell viability; controlled study; drug cytotoxicity; drug mechanism; drug selectivity; fibroblast culture; human; human cell; mouse; nonhuman; tumor cell line

**MeSH:** Adenosine-6'-N-ethylcarboxamide; Cell Line, Tumor; Cell Proliferation; Humans; Methotrexate; Receptor, Adenosine A<sub>1</sub>

*Medline is the source for the MeSH terms of this document.*

**Chemicals and CAS Registry Numbers:** 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyltetrazolium bromide, 298-93-1; 8-cyclopentyl-1,3-dipropylxanthine, 102147-07-7; adenosine 6'-N-ethylcarboxamide, 20920-29-9; cyclohexyladenosine, 33396-99-3; dimethyl sulfoxide, 67-68-0; phenylisopropyladenosine, 20120-40-0; Adenosine-6'-N-ethylcarboxamide, 20920-29-9; Methotrexate, 09-00-2; Receptor, Adenosine A<sub>1</sub>

**Manufacturers: Drug manufacturer:** Sigma Aldrich, Germany.