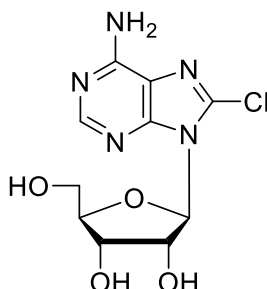


## Technical Information about 8-Chloroadenosine

**Cytotoxic metabolite of 8-Cl-cAMP**

Update: September 18, 2018 HJ



**Abbreviation:**

**8-Cl-Ado**

Formula	CAS No.	Molecular Weight	UV	BIOLOG Cat.No.
C <sub>10</sub> H <sub>12</sub> ClN <sub>5</sub> O <sub>4</sub>	[34408-14-5]	301.7	$\lambda_{\text{max}}$ 262 nm / $\epsilon$ 17000 / pH 7	C 006

**Name:** 8- Chloroadenosine ( 8-Cl-Ado )

**Description:** 8-Chloroadenosine is an analogue of adenosine where the hydrogen in position 8 of the heterocyclic nucleobase is replaced by a chlorine atom.

**Properties:** 8-Chloroadenosine is one of the main metabolites of the tumor growth inhibitor 8-chloro cyclic AMP (8-Cl-cAMP, BIOLOG Cat. No. C 007). In contrast to its corresponding bromo analog it shows relatively high cytotoxicity which could be due to different substrate properties towards adenosine deaminase.

**Specification:** Crystallized or lyophilized solid. Please keep in mind that equal amounts of the compound may look different in volume depending on humidity. The compound can even contract to small volume droplets. Normally the product is located in the conical bottom of the tube. Micromolar quantities are determined by UV at  $\lambda_{\text{max}}$ . Other metabolites of 8-Cl-cAMP and related structures are available as well: 8-Cl-cAMP (Cat. No. C 007), 8-Cl-5'-AMP (Cat. No. C 016), 8-Cl-ADP (Cat. No. C 042), 8-Cl-ATP (Cat. No. C 018), 8-Chloroadenine (Cat. No. C 023), Rp-8-Cl-cAMPS (Cat. No. C 011), Sp-8-Cl-cAMPS (Cat. No. C 012), 8-Cl-5'-IMP (on request), 8-Chloroinosine (Cat. No. C 019), 8-Chlorohypoxanthine (on request) and 8-Chloroxanthine (Cat. No. C 044).

**Purity:** Typical analysis is better than 98% (HPLC / UV / 262 nm). The product is not sterile and has not been tested for endotoxins.

**Solubility:** At room temperature the solubility of 8-Chloroadenosine in water is limited to approx. 16 mM. The compound is soluble to 22 mM in water with gentle warming to 35°C, and at 50°C a 100 mM solution can be achieved. When opening the tube please make sure that no substance is lost within the cap. Please rinse tube walls carefully and preferably use ultrasonic or vortex to achieve total and uniform mixing.

**Stability and Storage:** 8-Chloroadenosine has sufficient stability at room temperature and does not need special care during handling or shipment. Nevertheless, we recommend that the compound should be stored in the freezer, for longer storage periods preferably in freeze-dried form.

**Toxicity and Safety:** Since adenosine has multiple tasks in every organism, it is very likely that lipophilic analogues could interfere with many cell regulation processes *in vivo*. However, due to the rather small quantities to work with, no health hazards have been reported. Nevertheless please keep in mind that the *in vivo* properties of this compound are not sufficiently characterized up to now. Avoid skin contact or ingestion and allow only trained personnel to handle the product. Our products are designed, developed and sold for research purposes only. They are intended for *in vitro* and nonhuman *in vivo* laboratory applications. Any other use requires approval of health authorities.

**Not for drug, household or related uses!**

### Selected References for 8-Chloroadenosine:

Stellrecht, C.M.; Vangapandu, H.V.; Le, X.-F.; Mao, W.; Shentu, S., *J. Hematol. Oncol.*, **7**:23 (2014): "ATP Directed Agent, 8-Chloro-adenosine, Induces AMP Activated Protein Kinase Activity, Leading to Autophagic Cell Death in Breast Cancer Cells"

Jiao, Y.-Y.; Wang, X.-Q.; Lu, W.-L.; Yang, Z.-J.; Zhang, Q., *Eur. J. Pharmacol. Sci.*, **48**, 249 - 258 (2013): "A Novel Approach to Improve the Pharmacokinetic Properties of 8-chloro-adenosine by the Dual Combination of Lipophilic Derivatisation and Liposome Formulation"

Dennison, J.B.; Ayres, M.L.; Kaluarachchi, K.; Plunkett, W.; Gandhi, V., *J. Biol. Chem.*, **285**, 8022 - 8030 (2010): "Intracellular Succinylation of 8-Chloroadenosine and its Effect on Fumarate Levels"

Stanley, N.R.; Pattison, D.I.; Hawkins, C.L., *Chem. Res. Toxicol.*, **23**, 1293 - 1302 (2010): "Ability of Hypochlorous Acid and N-Chloramines to Chlorinate DNA and Its Constituents"

Waidmann, O.; Pleli, T.; Dvorak, K.; Baehr, C.; Mondorf, U.; Plotz, G.; Biondi, R.M.; Zeuzem, S.; Piiper, A., *J.Biol.Chem.*, **284**, 32256 - 32263 (2009): "Inhibition of the Equilibrative Nucleoside Transporter 1 and Activation of A2A Adenosine Receptors by 8-(4-Chlorophenylthio)-modified cAMP Analogs and their Hydrolytic Products"

Badouard, C.; Masuda, M.; Nishino, H.; Cadet, J.; Favier, A.; Ravanat, J.-L., *J. Chromatogr.*, **827**, 26 - 31 (2005): "Detection of Chlorinated DNA and RNA Nucleosides by HPLC Coupled to Tandem Mass Spectrometry as Potential Biomarkers of Inflammation"

Gandhi, V.; Chen, W.; Ayres, M.; Rhie, J.K.; Madden, T.L.; Newman, R.A., *Cancer Chemother. Pharmacol.*, **50**, 85 - 94 (2002): "Plasma and Cellular Pharmacology of 8-Chloro-Adenosine in Mice and Rats"

Gu, Y.-Y.; Zhang, H.-Y.; Zhang, H.-J.; Li, S.-Y.; Ni, J.-H.; Jia, H.-T., *Biochem. Pharmacol.*, **72**, 541 - 550 (2006): "8-chloro-adenosine Inhibits Growth at Least Partly by Interfering with Actin Polymerization in Cultured Human Lung Cancer Cells"

Lamb, D.; Steinberg, R.A., *J. Cell. Physiol.*, **192**, 216 - 224 (2002): "Anti-Proliferative Effects of 8-Chloro-cAMP and other cAMP Analogs Are Unrelated to Their Effects on Protein Kinase A Regulatory Subunit Expression"

Gandhi, V.; Ayres, M.; Halgren, R. G.; Krett, N. L.; Newman, R. A.; Rosen, S. T., *Cancer Res.*, **61**, 5474 - 5479 (2001): "8-Chloro-cAMP and 8-Chloro-Adenosine Act by the Same Mechanism in Multiple Myeloma Cells"

Yin, Y.-Z.; Allen, P.D.; Jia, L.; Kelsey, S.M.; Newland, A.C., *Leuk. Res.*, **25**, 423 - 431 (2001): "8-Cl-Adenosine Mediated Cytotoxicity and Sensitization of T-Lymphoblastic Leukemia Cells to TNF $\alpha$ -induced Apoptosis is via Inactivation of NF- $\kappa$ B"

Dransfield, D.T.; Griner, R.D.; Ray, S.; Keskinetepe, M.; Bollag, W.B., *J. Invest. Dermatol.*, **117**, 1588 - 1593 (2001): "8-Cl-Adenosine Induces Growth Arrest without Differentiation of Primary Mouse Epidermal Keratinocytes"

Bosanquet, A.G.; Burlton, A.R.; Bell, P.B.; Harris, A.L.; *Br. J. Cancer*, **76**, 511 - 518 (1997): "Ex Vivo Cytotoxic Drug Evaluation by DiSC Assay to Expedite Identification of Clinical Targets: Results With 8-Chloro-cAMP"

Langeveld, C.H.; Jongenelen, C.A.M.; Theeuwes, J.W.M.; Baak, J.P.A.; Heimans, J.J.; Stoof, J.C.; Peters, G.J.; *Biochem. Pharmacol.*, **53**, 141 - 148 (1997): "The Antiproliferative Effect of 8-Chloro-Adenosine, an Active Metabolite of 8-Chloro-Cyclic Adenosine Monophosphate, and Disturbances in Nucleic Acid Synthesis and Cell Cycle Kinetics"

Budillon, A.; Clair, T.; Hartmann, N.; Strong, J.; Sobukawa, Y.; Miki, K.; Worby, A.; Murray, K.J.; Cho-Chung, Y.S.; *Intern. J. Oncol.*, **9**, 1113 - 1120 (1996): "Novel Growth Inhibitory Effect of 8-Cl-cAMP is Dependent on Serum Factors that Modulate Protein Kinase A Expression But Not the Hydrolysis of 8-Cl-cAMP"

Barajas-Lopez, C.; Peres, A.L.; Espinosaluna, R.; *Amer. J. Physiol.*, **40**, C264 - C275 (1996): "Cellular Mechanisms Underlying Adenosine Actions on Cholinergic Transmission in Enteric Neurons"

Boe, R.; Gjertsen, B.T.; Døskeland, S.O.; Vintermyr, O.K.; *Br. J. Cancer* **72**, 1151 - 1159 (1995): "8-Chloro-cAMP Induces Apoptotic Cell Death in a Human Mammary Carcinoma Cell (MCF-7) Line"

Ruchaud, S.; Zorn, M.; Davilar-Villar, E.; Genieser, H.-G.; Hoffmann, C.; Gjertsen, B.T.; Døskeland, S.O.; Jastorff, B.; Lanotte, M., *Cell. Pharmacol.*, **2**, 127 - 140 (1995): "Evidence for Several Pathways of Biological Response to Hydrolysable cAMP-analogues Using a Model System of Apoptosis in IPC-81 Leukaemia Cells"

Lange-Carter, C.A.; Vuillequez, J.J.; Malkinson, A.M., *Cancer Res.*, **53**, 393 - 400 (1993): "8-Chloroadenosine Mediates 8-Chloro-Cyclic AMP-Induced Down-Regulation of Cyclic AMP-dependent Protein Kinase in Normal and Neoplastic Mouse Lung epithelial Cells by a Cyclic AMP-independent Mechanism"

Taylor, C.W.; Yeoman, L.C., *Anti-Cancer Drugs* **3**, 485 - 491 (1992): "Inhibition of Colon Tumor Cell Growth by 8-Chloro cAMP is Independent Upon its Conversion to 8-Chloroadenosine"

Langeveld, C.H. et al., *Cancer Res.*, **52**, 3994 - 3999 (1992): "Growth Inhibition of Human Glioma Cells Induced by 8-Chloroadenosine, an Active Metabolite of 8-Chloro Cyclic Adenosine 3':5' Monophosphate"

Cho-Chung, Y.-S. (Letter to the Editor)/Kessin, R.H. (Reply), *Cancer Res.*, **51**, 6206 - 6208 (1991): "Correspondence re: Van Lookeren Campagne et al., Ref. 4"

Pepe, S.; Tortora, G; Noguchi, P.D.; Marti, G.E.; Washington, G.C.; Cho-Chung, Y.S., *Cancer Res.*, **51**, 6263 - 6267 (1991): "Effects of 8-Chloradenosine 3',5'-Monophosphate and N6-Benzyl-Cyclic Adenosine 5'-Monophosphate on Cell Cycle Kinetics of HL-60 Leukemia Cells"

Van Lookeren Campagne et al., *Cancer Res.*, **51**, 6100 - 6105 (1991): "8-Cl-cAMP Inhibits the Growth of Chinese Hamster Ovary and Molt-4 Cells Through its Adenosine Metabolite"

Cho-Chung et al., *Cancer Investigation*, **7**, 161 - 177 (1989): "Site-selective CyclicAMP Analogs as New Biological Tools in Growth Control, Differentiation, and Proto-oncogene Regulation"

Bennett et al., *Nucleosides & Nucleotides*, **4**, 107 - 116 (1985): "Metabolism and Metabolic Effects of Halopurine Nucleosides in Tumor Cells in Culture"