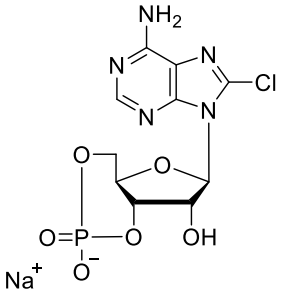
BIOLOG - LIFE SCIENCE INSTITUTE -

Technical Information about 8-Chloro-cAMP

Site selective activator of cAMP-depending protein kinase and tumor growth inhibitor

Update: July 03, 2018 HJ



Abbreviation: **8-Cl-cAMP**

Formula	CAS No.	Molecular Weight	UV	BIOLOG Cat. No.
$C_{10}H_{10}ClN_5O_6P{\cdot}Na$	[124705-03-9]	385.6	λ_{max} 262 nm / ε 17000 / pH 7	C 007

Name: 8- Chloroadenosine- 3', 5'- cyclic monophosphate (8-Cl-cAMP)

Description: 8-Cl-cAMP is an analogue of the natural signal molecule cyclic AMP in which the hydrogen in position 8 of the heterocyclic nucleobase is replaced by a chlorine atom.

Properties: 8-Cl-cAMP is a potent stimulator of cAMP-dependent protein kinases with high affinity for sites A and B of PKA type I. In addition it shows high site selectivity for site B of PKA type II. The analogue is degraded by cyclic nucleotide phosphodiesterases more slowly compared to natural cyclic AMP.
The increased lipophilicity which resembles 8-bromo cyclic AMP and Sp-cAMPS enables membrane permeability in several biosystems.
Due to its ability to stop growth of several cancer cell lines at very low doses, its therapeutic use is under investigation (Ref. 1-23, 26, 27). However, recent reports on active 8-Cl-metabolites showed that also degradation products could be responsible for cytostatic properties (Ref. 24, 25, 29-32). Therefore, BIOLOG offers an array of potential metabolites of 8-Cl-cAMP including 8-Cl-5'-AMP, 8-Cl-5'-ADP, 8-Cl-5'-ATP, 8-Cl-adenosine, 8-Cl-adenine, 8-Cl-5'-IMP, 8-Cl-inosine, 8-Cl-hypoxanthine and 8-Cl-xanthine and also the metabolically stable phosphorothioates Rp-/Sp-8-Cl-cAMPS (ref.28) (Cat. No.: C 003/C 004) are available.

Specification: Lyophilized or crystallized sodium salt. The free acid or other salt forms are available upon request. Equal concentrations of 8-Cl-cAMP can appear very different in volume due to sensitivity of the lyophilized form to 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 λ_{max}. 8-Cl-cAMP is also available in bulk amounts.

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

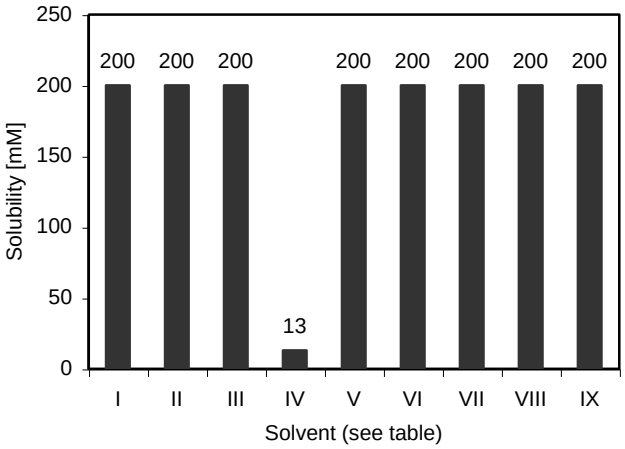
Stability and Storage: 8-Cl-cAMP is chemically stable under conditions of biological systems and media. Nevertheless, we recommend that the compound should be stored in the freezer, for longer storage periods preferably in freeze-dried form.

Toxicity and Safety: Since cyclic AMP has multiple tasks in every organism, it is very likely that lipophilic cAMP analogues will 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!

Solubility: Detailed information on the solubility of 8-Cl-cAMP in water and various buffers are listed in the solubility chart below. Concentrations have been tested at ambient temperatures and can be considered as minimum concentrations obtainable. 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.

BIOLOG Life Science Institute, Bremen, Germany Phone: 49 (0) 421 591355 Fax: 49 (0) 421 5979713 e-mail: service@biolog.de

No.	Solvent	Solubility [mM]
I	H_2O	200
II	DMSO	200
III	DMF	200
IV	Ethanol 96%	13
V	Methanol	200
VI	PBS, pH 7.4	200
VII	100 mM Na_2HPO_4, pH 7.0	200
VIII	25 mM Hepes/NaOH, pH 7.2	200
IX	25 mMTris/HCl, pH 7.4	200



Selected References for 8-Cl-cAMP:

Due to limited space we cannot cite all references for 8-Cl-cAMP. If you do not find the information needed, please ask for a computer search in our reference and application data bank. For an extended reference list please refer to our website http://www.biolog.de. Since we permanently collect all data available, we appreciate receiving respective information such as citations, reprints or accepted manuscripts as well as unpublished application reports.

Jäger, R.; Russwurm, C.; Schwede, F.; Genieser, H.-G.; Koesling, D.; Russwurm, M., *J. Biol. Chem*., **287**, 1210 - 1219 (2012): „ Activation of PDE10 and PDE11 Phosphodiesterases“

Scott, S.-P.; Shea, P.W.; Dryer, S.E., *Biochemistry*, **46**, 9417 - 9431 (2007): "Mapping Ligand Interactions with the Hyperpolarization Activated Cyclic Nucleotide Modulated (HCN) Ion Channel Binding Domain Using a Suluble Construct"

Moll, D.; Prinz, A.; Gesellchen, F.; Drewianka, S.; Zimmermann, B.; Herberg, F.W., *J. Neural. Transm*., **113**, 1015 - 1032 (2006): “Biomolecular Interaction Analysis in Functional Proteomics”

Weissinger, E.M.; Oettrich, K.; Genieser, H.-G.; Schwede, F.; Dangers, M.; Dammann, E.; Kolb, H.-J.; Mischak, H.; Ganser, A.; Kolch, *W., British. J. Cancer*, **91**, 186 - 192 (2004) : “Activation of Protein Kinase A (PKA) by 8-Cl-cAMP as a Novel Approach for Antileukaemic Therapy”

Guillemin, M.-C.; Raffoux, E.; Vitoux, D.; Kogan, S.; Soilihi, H.; Lallemand-Breitenbach, V.; Zhu, J.; Janin, A.; Daniel, M.-T.; Gourmel, B.; Degos, L.; Dombret, H.; Lanotte, M.; de Thé, H., *J. Exp. Med.*, **196**, 1373 - 1380 (2002): "In Vivo Activation of cAMP Signaling Induces Growth Arrest and Differentiation in Acute Promyelocytic Leukemia"

Grbovic, O.; Jovic, V.; Ruzdijic, S.; Pejanovic, V.; Rakic, L.; Kanazir, S., *Cancer Invest.*, **20**, 972 - 982 (2002): "8-Cl-cAMP Affects Glioma Cell-Cycle Kinetics and Selectively Induces Apoptosis"

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”

Schwede, F.; Maronde, E.; Genieser, H.-G.; Jastorff, B., *Pharmacol. Ther.*, **87**, 199 - 226 (2000): "Cyclic Nucleotide Analogs as Biochemical Tools and Prospective Drugs"

Vintermyr, O.K.; Bøe, R.; Brustugun, O.T.; Maronde, E.; Aakvaag, A.; Døskeland, S.O., *Endocrinology*, **136**, 2513 - 2520 (1995): "Cyclic Adenosine Monophosphate (cAMP) Analogs 8-Cl- and 8-NH_2-cAMP Induce Cell Death Independently of cAMP Kinase-Mediated Inhibition of the G_1/S Transition in Mammary Carcinoma Cells (MCF-7)"

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

Cho-Chung, Y.S.; Clair, T., *Pharmac. Ther*., **60**, 265 - 288 (1993): "The Regulatory Subunit of cAMP-dependent Protein Kinase as a Target for Chemotherapy of Cancer and Other Cellular Dysfunctional-related Diseases"

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”

References cited in this Technical Information:

32 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"

31 Cho-Chung, Y.S., *Biochem. Soc. Trans*., **20**, 425 - 430 (1992): "Suppression of Malignancy Targeting Cyclic AMP Signal Transducing Proteins"

BIOLOG Life Science Institute, Bremen, Germany Phone: 49 (0) 421 591355 Fax: 49 (0) 421 5979713 e-mail: service@biolog.de

30 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"

29 Langeveld, C.H.; Jongenelen, C.A. M.; Heimans, J.J.; Stoof, J.C., *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"

28 Yokozaki, H.; Tortora, G.; Pepe, S.; Maronde, E.; Genieser, H.-G.; Jastorff, B.; Cho-Chung, Y.S., *Cancer Res*., **52**, 2504 - 2508 (1992): "Unhydrolysable Analogs of Cyclic Adenosine-3',5'-Monophosphate Demonstrating Growth Inhibition and Differentiation in Human Cancer Cells"

27 Cho-Chung, Y.-S.; Clair, T.; Tortora, G.; Yokozaki, H., *Pharmac. Ther*., **50**, 1 - 33 (1991): "Role of Site-selective cAMP Analogs in the Control and Reversal of Malignancy"

26 Yokozaki, H. et al., *Proc. Amer. Assoc. Cancer Res*., (1991) in press: "Site-selective cAMP Analogs Inhibit the Growth of Multidrug Resitstant Cell Lines and Suppress the Expression of P-Glycoprotein"

25 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. 24

24 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"

23 Ciardiello, F.; Tortora, G.; Kim, N.; Clair, T.; Ally, S.; Salomon, D. S.; Cho-Chung, Y.S., J. Biol. Chem., **265**, 1016 - 1020 (1990): "8-Chloro-cAMP Inhibits Transforming Growth Factor A Transformation of Mammary Epithelial Cells by Restoration of the Normal mRNA Patterns for cAMP- dependent Protein Kinase Regulatory Subunit IsoformsWhich Show Disruption upon Transformation"

22 Tortora et al.; *Proc. Amer. Assoc. Cancer Res*., **31**, 38 (1990), Abstr. 221: "Synergistic Effect of rhGM-GSF and Site-selective 8-Cl-cAMP on the Differentiation of HL-60 Human Promyelocytic Leukemic Cells"

21 Dixit, R. et al., Proc. *Amer. Assoc. Cancer Res*., **31**: (Abstr. 2275) 384 (1990): "Kinetics and Toxicity of 8-Chloroadenosine- 3', 5'-cyclic monophosphate (8-Cl-cAMP) in Beagle Dogs"

20 Cho-Chung, Y.S., *Cancer Res*., **50**, 7093 - 7100 (1990): "Role of Cyclic AMP Receptor Proteins in Growth, Differentiation, and Suppression of Malignancy: New Approaches to Therapy"

19 Yokozaki, H.; Clair, T.; Mednieks, M.; Tortora, G.; Ally, S.; Merlo, G.; Cho-Chung, Y.S., *Proc. Am. Assoc. Cancer Res*.,**30**, 446 (1989): "Nuclear Translocation of the Regulatory Subunit of Type II Protein Kinase Correlates With Increased DNA (CRE)-Protein Binding Activity in Human Cancer Cell Lines Treated With Site-Selective Analogs of cAMP"

18 Cho-Chung, Y.S.; Clair, T.; Tagliaferri, P.; Ally, S.; Katsaros, D.; Tortora, G.; Neckers, L.; Avery, T.L.; Crabtree, G.W.; Robins, R.K., *Cancer Investigation*, **7**, 161 - 177 (1989): "Site-selective Cyclic AMP Analogs as New Biological Tools in Growth Control, Differentiation, and Proto-oncogene Regulation"

17 Ally, S.; Clair, T.; Katsaros, D.; Tortora, G.; Yokozaki, H.; Finch, R.A.; Avery, T.L.; Cho-Chung, Y.S., *Cancer Res*., **49**, 5650 - 5655 (1989): "Inhibition of Growth and Modulation of Gene Expression in Human Lung Carcinoma in Athymic Mice by Site-selective 8-Cl-Cyclic Adenosine Monophosphate"

16 Mednieks et al., *FEBS Lett*., **254**, 83 - 88 (1989): "Site-selective 8-Chloro-cAMP Which Causes Growth Inhibition and Differentiation Increases DNA (CRE) Binding Activity in Cancer Cells"

15 Cho-Chung, Y.S., *J. Natl. Cancer Inst*., **81**, 982 - 987 (1989): "Site-selective 8-Chloro-Cyclic Adenosine 3', 5'- Monophosphate as a Biological Modulator of Cancer: Restoration of Normal Control Mechanisms"

14 Tortora et al., *Proc. Natl. Acad. Sci. USA*, **86**, 2849 - 2852 (1989): "Induction of Megakaryocytic Differentiation and Modulation of Protein Kinase Gene Expression by Site-selective cAMP Analogs in K-562 Human Leukemic Cells"

13 Tortora, G.; Ciardiello, F.; Ally, S.; Clair, T.; Salomon, D. S.; Cho-Chung, Y. S., *FEBS Lett*., **242**, 363 - 367 (1989): "Site-selective 8-Chloroadenosine 3', 5'-Cyclic Monophosphate Inhibits Transformation and Transforming Growth Factor A Production in Ki-ras-Transformed Rat Fibroblasts"

12 Robins, R.K.; Revankar, G.R.; Chang,Y., *Int. Patent Appl.PCT/US88/01217, Int. Filing Date April 20,* 1988: "Treatment of Malignant Tumors with 8-Chloroadenosine 3', 5'- Cyclic Phosphate, 8-Aminoadenosine 3', 5'-Cyclic Phosphate and Preparation Thereof"

11 Avery et al., *Proc. Am. Assoc. Cancer Res*., **29**, 354 (1988): "Treatment of Murine and Human Neoplasms in vivo With the Site-selective cAMP Analog, 8-CL-cAMP"

10 Cho-Chung et al., *J. Cell Biol.*, **107**, 492a (1988): "Nuclear Location Signal and Nuclear Translocation of Type II Protein Kinase Regulatory Subunit in Site- Selective cAMP-Analog-Induced Growth Control and Differentiation"

9 Tagliaferri, P.; Katsaros, D.; Clair, T.; Ally, S.; Tortora, G.; Neckers, L.; Rubalcava, B.; Parandoosh, Z.; Chang, Y.A.; Revankar, G.R.; Crabtree, G.W.; Robins, R.K.; Cho-Chung, Y.-S., *Cancer Res*., **48**, 1642 - 1650 (1988): "Synergistic Inhibition of Growth of Breast and Colon Human Cancer Cell Lines by Site-selective Cyclic AMP Analogs"

8 Ally, S.; Tortora, G.; Clair, T.; Grieco, D.; Merlo, G.; Katsaros, D.; Øgreid, D.; Døskeland, S. O.; Jahnsen, T.; Cho-Chung, Y.S., *Proc. Natl. Acad. Sci. USA*, **85**, 6319 - 6322 (1988): "Selective Modulation of Protein Kinase Isozymes by the Site-selective Analog 8-Chloroadenosine- 3', 5'- Cyclic Monophosphate Provides a Biological Means for Control of Human Colon Cancer Cell Growth"

BIOLOG Life Science Institute, Bremen, Germany Phone: 49 (0) 421 591355 Fax: 49 (0) 421 5979713 e-mail: service@biolog.de

7 Rubalcava et al., *Proc. 79. Ann. Meet. Amer. Assoc. Cancer Res. New Orleans*, **29**, 358 (1988): "8-Chloro and 8-Amino cAMP Translocate Protein Kinase C from Plasma Membrane to Cytosol in Cancer Cells"

6 Parandoosh et al., *Proc. 79. Ann. Meet. Amer. Assoc. Cancer Res. New Orleans*, **29**, 345 (1988): "Diacylglycerol (DAG) Mass Measurement in Tumor Cells Treated with 8-Chloro cAMP"

5 Katsaros et al., *Int. J. Cancer,* **41**, 863 - 867 (1988): "Site-selective Cyclic AMP Analogs Are Antagonistic to Estrogen Stimulation of Growth and Proto-oncogene Expression in Human Breast-cancer Cells"

4 Tortora, G.; Ciardiello, F.; Ally, S.; Clair, T.; Salomon, D. S.; Cho-Chung, Y.S., *Blood*, **71**, 230 - 233 (1988): "Site-selective Cyclic AMP Analogs at Micromolar Concentrations Induce Growth Arrest and Differentiation of Acute Promyelocytic, Chronic Myelocytic, and Acute Lymphocytic Human Leukemia Cell Lines"

3 Tagliaferri, P.; Katsaros, D.; Clair, T.; Neckers, L.; Robins, R.K.; Cho-Chung, Y.S., *J. Biol. Chem*., **263**, 409 - 416 (1988): "ReverseTransformation of Harvey Murine Sarcoma Virus-transformed NIH/3T3 Cells by Site-selective Cyclic AMP Analogs"

2 Clair, T.; Ally, S.; Tagliaferri, P.; Robins, R. K.; Cho-Chung, Y.S., *FEBS Lett*., **224**, 377 - 384 (1987): "Site-selective Cyclic AMP Analogs Induce Nuclear Translocation of the RII cAMP Receptor Protein in Ha-MuSV-Transformed NIH/3T3 Cells"

1 Katsaros, D.; Tortora, G.; Tagliaferri, P.; Clair, T.; Ally, S.; Neckers, L.; Robins, R.K.;Cho-Chung, Y.S., *FEBS Lett.,* **223**, 97 - 103 (1987): "Site-selective Cyclic AMP Analogs Provide a New Aproach in the Control of Cancer Cell Growth"

BIOLOG Life Science Institute, Bremen, Germany Phone: 49 (0) 421 591355 Fax: 49 (0) 421 5979713 e-mail: service@biolog.de