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Technical Information about Rp-8-Piperidino-cAMPS

Site selective, PDE-resistant and membrane permeant inhibitor of protein kinase A

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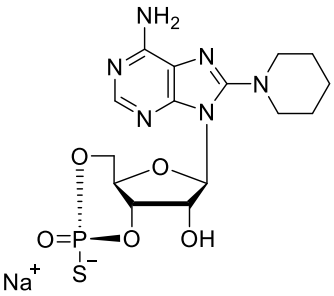

Abbreviation: **Rp-8-PIP-cAMPS**

Formula	CAS No.	Molecular Weight	UV	BIOLOG Cat.No.
$C_{15}H_{20}N_6O_5PS{\cdot}Na$	[156816-36-3]	450.4	λ_{max} 273.5 nm / ε 15000 / pH7	P 004

Name: 8- Piperidinoadenosine- 3', 5'- cyclic monophosphorothioate, Rp-isomer

Description: Rp-8-PIP-cAMPS is an analogue of the parent compound cyclic AMP in where the equatorial one of the two exocyclic oxygen atoms in the cyclic phosphate moiety is modified by sulfur (the suffix "p" indicates that R/S nomenclature refers to phosphorus). In addition, the hydrogen in position 8 of the nucleobase is replaced by a piperidine ring.
Its synthesis and distribution is protected by patent DE 3802865.4, licensed to BIOLOG Life Science Institute.

Properties:

- **inhibitor of protein kinase A (PKA)**[1]
- **high site selectivity, prefering site B of PKA II**
- **metabolic stability towards cyclic nucleotide- responsive phosphodiesterases due to phosphorothioate modification**
- **high lipophilicity and good membrane permeability while still soluble in aqueous solvents**

Rp-8-PIP-cAMPS is a site- selective, lipophilic analogue of the phosphodiesterase-stable protein kinase A inhibitor Rp-cAMPS which strongly selects site B of PKA type II. By occupying cAMP binding sites Rp-8-PIP-cAMPS prevents the kinase holoenzyme from dissociation and thus from activation. Due to this working principle, preincubation of the inhibitor prior to the activation step is necessary for optimal results. Rp-8-PIP-cAMPS is about 11 times more lipophilic compared to Rp-cAMPS.

Application: Experience shows that applicable concentrations of Rp-8-PIP-cAMPS depend on the type of biosystem, its membrane properties and kinase content. A main application for Rp-8-PIP-cAMPS is to eliminate the first messenger-stimulated phosphorylation by cyclic AMP-dependent protein kinase. For this purpose preincubation (e.g. 20 min.) is important, since the production of intracellular cyclic AMP initiated by a first messenger is much faster than the antagonist can penetrate the membrane when given extracellularly. Since Rp-8-PIP-cAMPS is metabolically stable in mammalian and many other systems, there is no danger of degradation during incubation periods.

Specification: Lyophilized or crystallized sodium salt.The free acid or other salt forms are available upon request.
Equal amounts of Rp-8-PIP-cAMPS can appear very different in volume due to high sensitivity of the lyophilized form to humidity and 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}. The agonistic Sp- isomer (Sp-8-PIP-cAMPS) is offered by BIOLOG as well (Cat. No. P 005).

Purity: Typical analysis is better than 99% (HPLC /UV/273 nm). The product is not sterile.
Caution: Since even minor impurities of 8-PIP-cAMP (0.2%) or Sp-8-PIP-cAMPS can already activate protein kinase and compete with the antagonistic effect of the Rp- isomer, it is very important to work with strictly pure compounds concerning cyclic nucleotide contaminants. Therefore, Rp-8-PIP-cAMPS is specially checked for absence of both, 8-PIP-cAMP and Sp-8-PIP-cAMPS (< 0.05% when packed). However, we cannot guarantee total absence of 8-PIP-cAMP due to its formation during prolonged storage.

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Solubility: Rp-8-PIP-cAMPS is readily soluble in water or buffer. Please rinse tube walls carefully (and cap if necessary) and preferably use ultrasonic or vortex to achieve total and uniform mixing. When opening the tube make sure that no substance is lost within the cap.

Stability and Storage: Rp-8-PIP-cAMPS has sufficient stability at room temperature and does not need special care during handling or shipment. Nevertheless the compound and its solutions should be stored in the refrigerator and should be lyophilized and frozen for longer storage periods since desulfurization yielding 8-PIP-cAMP can occur slowly. This normally rather slow sulfur/oxygen exchange is accelerated by oxidizing agents.

Toxicity and Safety: Since cyclic AMP has multiple tasks in every organism it is very likely that lipophilic cAMP analogs 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 these compounds 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 Rp-8-PIP-cAMPS:

For a detailed list please inquire or visit our website http://www.biolog.de)

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