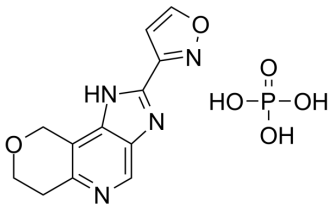
S-8510 phosphate

Cat. No.:	HY-103225
CAS No.:	151466-23-8
Molecular Formula:	$C_{12}H_{13}N_4O_6P$
Molecular Weight:	340.23
Target:	GABA Receptor
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	S-8510 (phosphate) is an inverse Benzodiazepine (BDZ) receptor agonist, with K_is of 34.6 nM, 36.2 nM for –GABA and +GABA respectively.
IC_{50} & Target	Ki: 34.6 nM (-GABA), 36.2 nM (+GABA)[1].
In Vitro	S-8510 has a relatively high affinity to BDZ receptors. The ratio of Ki values for each ligand with and without GABA is defined as the GABA ratio, which is considered as a biochemical index for BDZ receptor ligands. The GABA ratio for S-8510 or CGS8216 is close to the value for flumazenil which is considered as an antagonist or a very weak agonist. S-8510 (10^{-7} M) enhances LTP and this enhancement is antagonized by BDZ receptor antagonist, flumazenil. Flumazenil itself does not atfect LTP or evokes responses prior to tetanic stimulation. S-8510 has no effect on the field evoked potential up to 10^{-5} M. However, S-8510 increases the amplitude of the population spike at a dose of 10^{-4} M, and this effect is completely antagonized by concomitant application of flumazenil (10^{-4} M) [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	S-8510 or CGS8216 could cause lethal convulsion only in combination with more than 90 mg/kg of PTZ. The proconvulsant activity of S-8510 appears to be selective for PTZ-induced subconvulsive state. Scopolamine decreases the time spending in the area around the platform, indicating the amnesic action of scopolamine. S-8510 and CGS8216 reverses this scopolamine-induced amnesia. S-8510 improves the memory impairment induced by diazepam in the water maze and passive avoidance paradigms as well. S-8510 dose-dependently increases the ACh level up to 100 mg/kg. Both S-8510 and PTZ increases the extracellular level of NA in the hippocampus in a dose-dependent manner. Anxiogenic actions of S-8510, CGS8216 and FG7142 are examined in the water lick conflict paradigm of Wistar rats. S-8510 and CGS8216 fail to affect this behavioral paradigm up to 30 mg/kg. S-8510 significantly decreases the immobility time in the forced swimming test using ddY mice at 40 to 80 mg/kg in a dose-dependent manner. In the tetrabenazine-induced ptosis model, S-8510 significantly reduces the extent of ptosis induced by tetrabenazine at doses more than 10 mg/kg. Again, S-8510 reduces the extent of ptosis only by 39% even at the maximum dose, whereas imipramine exerts more pronounced effects (by about 80% at a dose of 20 mg/kg)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal	Mice, Rats[1]

Administration [1]	Proconvulsant actions of S-8510 are examined in combiition with a subconvulsive dose of convulsant (PTZ or strychnine) or minimal electroconvulsive shock in ddY mice. Each convulsant is administrated, simultaneously with the inverse agonist, whereas minimal electroconvulsive shock is applied 5 min after intravenous injection of the inverse agonist. The proconvulsant test of S-8510 on PTZ (52, 62.5, 75 or 90 mg/kg s.c.) or strychnine (0.25 mg/kg, s.c.)-induced convulsion is made. ED_{50} values for producing clonic convulsion to death in 50% of ddY mice are calculated. Anxiogenic actions of each inverse agonist are examined in the punished water licking method in Wistar rats. Each inverse agonist is administered per OS 30 min before the test trial. Antiamnesic actions of inverse agonists are examined in the water maze paradigm. Wistar rats are given 4 trials every day for consecutive 4 days. On the 5 th day, each animal has the retention test for 60 s. Amnesia is produced by intraperitoneally injected scopolamine at a dose of 0.5 mg/kg. Scopolamine and each inverse agonist are given 15 min and 30 min before the retention trial, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Kawasaki K, et al. A novel benzodiazepine inverse agonist, S-8510, as a cognitive enhancer. Prog Neuropsychopharmacol Biol Psychiatry. 1996 Nov;20(8):1413-25.

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