Product Data Sheet

Product Name: MHP 133
Cat. No.: GC30446

Chemical Properties

Cas. No.	147340-43-0		
SMILES	O=C(N/N=C/C1=C(OC(N(C)C)=O)C=CC=[N+]1C)NC2=CC=CC=C2.[Cl-]		
Formula	$C_{17}H_{20}ClN_5O_3$	M.Wt	377.83
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	MHP 133		

Protocol

Kinase experiment:

Rat cerebral cortex is homogenized in ice cold 50 mM Tris-HCl buffer containing 120 mM NaCl, 5 mM KCl, 1 mM MgCl2, and 2 mM CaCl2 (pH 7.0). The homogenate is centrifuged at 37,200 g for 20 min at 0°C. The pellet is washed twice and resuspended in fresh buffer. For nicotinic receptor binding, [3H]cytisine is incubated with 0.5 mg protein and various concentrations of MHP-133 or other ligand in a final volume of 250 µL ta 4°C for 120 min. About 10 µM (-)-nicotine is used to determine nonspecific binding. Bound radioactivity is isolated by rapid filtration through polyethyleneimine-treated glass fiber filters and by washing several times with icecold buffer (Tris-HCl, 50 mM). Filters are soaked in scintillation fluor for 6 h prior to quantification or radioactivity in a scintillation counter. Data are presented in triplicate.

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Cell experiment:

PC-12 cells are maintained in 150-cm2 tissue-culture flasks in Dulbecco's modified Eagles medium containing 7% horse serum, 7% fetal calf serum, 1% nonessential amino-acids and 1% streptomycin (DMEM). The cells are incubated at 37°C in a 5% CO2-enriched, humidified atmosphere. For the actual experiments PC-12 cells are plated on poly-L-lysine coated 24-well plates at a density of 40,000 cells per well in DMEM medium containing 50 ng/mL nerve growth factor (NGF). To attain maximum differentiation, the cells are maintained in DMEM.NGF medium for 7 days with the medium being changed every 2 or 3 days. Next, the differentiated cells are incubated with vehicle or with a test drug (prepared in serum-free DMEM media with no exogenous NGF) for 24 h. A parallel set of control cells are maintained in DMEM.NGF medium in each experiment. Cell viability (cytotoxicity) is determined by using the Cell Titer 96 cell proliferation/cytotoxicity assay kit, which is based on the cellular conversion of a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenltetrazolium bromide (MTT) into a formazan product that can be detected spectrophotometrically. At the completion of the incubation period, the culture medium is aspirated and 15 µL of dye solution in DMEM is added. After 4 h at 37°C, 100 µL of solubilization/stop solution is added and the absorbance of solubilized MTT formazan products is measured at 579 nm. All data are normalized to untreated control cells in each plate.

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Animal experiment:

Male Sprague-Dawley, outbred Wistar rats weighing 250-300 g are housed separately in our animal care facility for 1 week prior to experimentation. At the time of the experiment the 40 animals are randomLy assigned to one of four treatment groups, a saline vehicle group, or a group to be administered 50, 100 or 200 μg/kg of MHP-133. Vehicle (1 mL/kg body weight) is administered i.p. 30 min prior to testing in the Morris Water Maze apparatus. The apparatus consists of a water-filled (room temperature) tub 1.2 m in diameter. A mounting platform is fixed in place and slightly submerged in the northwest quadrant of the tub. The platform is similar in color to the inner surface of the tub so as to make it difficult to visualize. The tub is always maintained in the same orientation with respect to visual cues placed on the walls, around the testing room. Rats are tested by placing the animal in the water facing away from the platform. Four consecutive trials are administered with 10 min between trials. In each successive trial the rats are placed first in the south quadrant of the tub, followed by the north, east and west quadrants. The time required for the rat to find (place at least 2 paws on) the platform is monitored to the nearest 0.1 s. All rats found the platform in less than 90 s.

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References:

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Background

a drug with multiple CNS targets, and inhibits acetylcholinesterase (AChE) with Ki of 69 μM; also active against muscarinic M1 and M2 receptors, serotonin 5HT4 receptors, and imidazole I2 receptors.

MHP-133 is be active (>50% displacement or activity) against muscarinic M1 and M2 receptors, serotonin 5HT4 receptors, and imidazole I2 receptors. MHP-133 exhibits this nicotinic-like activity in the cell line. Although the ED50 for inducing TrkA expression is only about 1 μM, it does predicts the cytoprotective action of MHP-133 in differentiated PC-12 cells deprived of growth factor for 24 h. MHP-133 (10-100 μM) significantly increases the levels of sAPP from cultured astrocytes by 40-60%. MHP-133 produces a bi-phasic effect on slice survival, particularly in the dentate gyrus and the CA1 regions[1].

In rats, MHP-133 (50, 100, or 200 μg/kg, i.p.) enhances acquisition of the task and increases task accuracy. MHP-133 elicits significant improvements in task accuracies during sessions initiated 10 min after dosing[1].

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