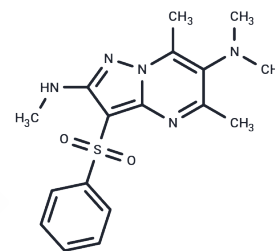


AVN-492

Chemical Properties

CAS No. : 1220646-23-0
 Formula: C17H21N5O2S
 Molecular Weight: 359.45
 Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.



Biological Description

Description	AVN-49 is a potent and selective 5-HT6R Antagonist (Ki: 91 pM).
Targets(IC50)	5-HT Receptor
In vitro	Affinity of AVN-492, K_i^{b} , to compete with [3H]LSD for binding to 5-HT6R was estimated to be 91 pM ($IC_{50}^{b} = 194$ pM). Affinity of 509 AVN-492 to the 5-HT2BR, $K_i^{b} = 170$ nM ($IC_{50}^{b} = 268$ nM) was more than three orders of magnitude lower. Despite being metabolized by human microsomes, AVN-492 did not appreciably inhibit five major human recombinant CYP isoforms, CYP3A4, 1A2, 2C9, 2C19, and 2D6 at concentrations as high as 10 M [1].
In vivo	AVN-492 has high oral bioavailability and good brain permeability in rodents. In behavioral tests, AVN-492 shows an anxiolytic effect in the elevated plus-maze model, prevents an apomorphine-induced disruption of startle pre-pulse inhibition (the PPI model) and reverses scopolamine- and MK-801-induced memory deficit in passive avoidance model. No anti-obesity effect of AVN-492 was found in a murine model [1].
Kinase Assay	Assessment of AVN-492 selectivity was performed on a panel of 69 therapeutic targets including receptors, ion channels, neuromediator transporters, and enzymes. The full list of the targets is presented in the Supplementary Material. AVN-492 interactions with therapeutic targets were assessed by either equilibrium competitive displacement of corresponding radiolabeled ligands or inhibition of corresponding enzymatic activities. The studies were performed at Eurofins in accordance with their internally optimized procedures as briefly described in. The displacement of radioligands and inhibition of enzymatic activities were measured at AVN-492 concentration of 1 M in duplicates. Affinities of AVN-492 to both the 5-HT6R and 5-HT2BR were assessed in an equilibrium competitive [3H]LSD displacement assay. AVN-492 was provided at different concentrations and [3H]LSD was kept at a concentration of 1.50 nM for 5-HT6R, or 1.20 nM for 5-HT2BR. The ligands were added to corresponding receptor-membrane suspensions (plasma membranes obtained from engineered HeLa cells expressing recombinant human 5-HT6R or engineered CHO-K1 cells expressing recombinant human 5-HT2BR). The cell membrane/ligands mixtures were incubated in buffer of the following composition: For 5-HT6R: 50 mM Tris-HCl, pH 7.4, 150 mM NaCl, 2 mM ascorbic acid, 0.001% BSA - 120 min at 37°C; for 5-HT2BR: 50 mM Tris-HCl, pH 7.4, 4 mM CaCl ₂ , 0.1% ascorbic acid - 60 min at 37°C. Specific radio-ligand binding was measured as a

Kinase Assay	difference between total binding and binding in the presence of excessive concentration of cold serotonin [1].
Animal Research	For pharmacokinetic, behavior, and toxicity studies, male Wistar rats (220-242 g), male CD1 mice (24-30 g), male SHK mice (20-25 g), and male Balb/C mice (15-20 g) were used. Rodents were obtained from Jackson Laboratories and housed in a standard laboratory animal facility in groups of 5-7 animals per cage. Before entering the investigation, the animals were acclimated at least for seven days. Obese C57BL/6 male 18-week-old mice were obtained from Jackson Laboratories. The mice were fed on a high-fat diet (60% kcal Research Diet 12492i) from the age of 6 weeks. Upon arrival, the mice were maintained on the same high fat diet with free access to both food and water. The mice were individually housed in solid bottom static isolators with Bed-O'Cobs? bedding inside a BioBUBBLE? clean room that provided HEPA-filtered air into the clean room environment at a rate of 100 complete air changes per hour. All treatments and procedures including body weight determinations, drug administration, and glucose measurements were carried out in the clean room environment [1].

Solubility Information

Solubility	DMSO: 7.5 mg/mL (20.87 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (2.78 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.782 mL	13.9101 mL	27.8203 mL
5 mM	0.5564 mL	2.782 mL	5.5641 mL
10 mM	0.2782 mL	1.391 mL	2.782 mL
50 mM	0.0556 mL	0.2782 mL	0.5564 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Ivachtchenko AV, et al. AVN-492, A Novel Highly Selective 5-HT6R Antagonist: Preclinical Evaluation. J Alzheimers Dis. 2017;58(4):1043-1063.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481