

Product Data Sheet

Product Name: AR-A014418

Cat. No.: GC15425

Chemical Properties

Cas. No. 487021-52-3

Chemical Name 1-[(4-methoxyphenyl)methyl]-3-(5-nitro-1,3-thiazol-2-yl)urea

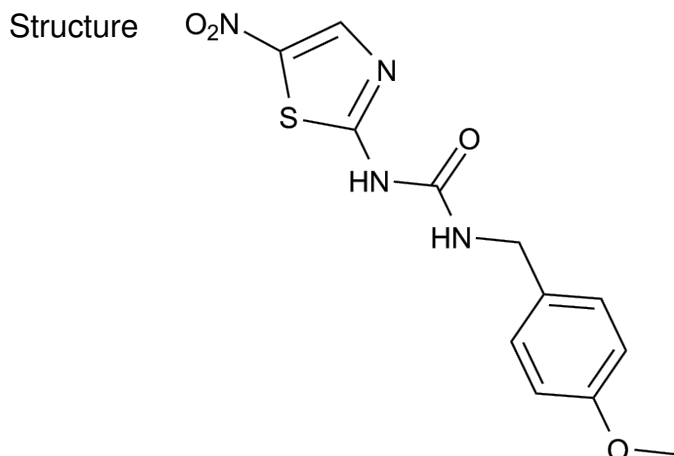
SMILES COC1=CC=C(C=C1)CNC(=O)NC2=NC=C(S2)[N+](=O)[O-]

Formula $C_{12}H_{12}N_4O_4S$ M.Wt 308.31

Solubility ≥ 15.4 mg/mL in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.



Protocol

Kinase experiment [1]:

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Kinase assays

The competition experiments were carried out in duplicate with 10 concentrations of the inhibitor. The biotinylated peptide substrate was added at 2 μ M in an assay buffer containing 6 milliunits of recombinant human GSK3, 12 mM MOPS, pH 7.0, 0.3 mM EDTA, 0.01% β -mercaptoethanol, 0.004% Brij 35, 0.5% glycerol, and 0.5 μ g of bovine serum albumin/25 μ l and preincubated. The reaction was initiated by the addition of 0.04 μ Ci of [^{33} P]ATP and unlabeled ATP in 50 mM Mg(Ac) $_2$ to a final concentration of 1 μ M ATP and assay volume of 25 μ l. After incubation for 20 min at room temperature, each reaction was terminated by the addition of 25 μ l of stop solution containing 5 mM EDTA, 50 μ M ATP, 0.1% Triton X-100, and 0.25 mg of streptavidin-coated SPA beads corresponding to 35 pmol of binding capacity.

Cell experiment [1]:

Cell lines

3T3 fibroblasts were engineered to stably express four-repeat tau protein

Preparation method

The solubility of this compound in DMSO is >15.4 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting condition 100 nM to 50 μ M for 24 h

Applications

AR-A014418 could inhibit the tau phosphorylation at a GSK3-specific site in cells that were stably expressing human four-repeat tau protein. AR-A014418 could also protect N2A neuroblastoma cells against cell death, which was mediated through inhibition of the phosphatidylinositol 3-kinase/protein kinase B survival pathway.

Animal experiment [2]:

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Animal models Male Sprague–Dawley rats

Dosage form 30 µmol/kg, i.p.

Application The subacute intraperitoneal injections of AR-A014418 reduced immobility time in rats exposed to the forced swim test, a well-established model for antidepressant efficacy. In addition, the specificity of this effect was supported by the finding that AR-A014418 could decrease both spontaneous and amphetamine-induced activity.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1] Bhat R, Xue Y, Berg S, Hellberg S, Orm M, Nilsson Y, Radester AC, Jerning E, Markgren PO, Borgegrd T, Nyf M, Giménez-Cassina A, Hernández F, Lucas JJ, Díaz-Nido J, Avila J. Structural insights and biological effects of glycogen synthase kinase 3-specific inhibitor AR-A014418. J Biol Chem. 2003;278(46):45937-45.

[2] Gould TD, Einat H, Bhat R, Manji HK. AR-A014418, a selective GSK-3 inhibitor, produces antidepressant-like effects in the forced swim test. Int J Neuropsychopharmacol. 2004;7(4):387-90.

Background

IC50: 104 ± 27 nM

Glycogen synthase kinase 3 (GSK3) is a serine/threonine kinase that has been implicated in pathological conditions such as diabetes and Alzheimer's disease (AD). AR-A014418 is a selective GSK-3 inhibitor.

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In vitro: ARA014418 acted as an ATP-competitive manner and did not significantly inhibit cdk2 or cdk5 or 26 other kinases demonstrating high specificity for GSK3. AR-A014418 inhibited tau phosphorylation at a GSK3-specific site (Ser-396) in cells stably expressing human four-repeat tau protein [1].

In vivo: ARA014418 induced behavioural changes that were consistent with the effects of antidepressant drugs. Subacute intraperitoneal injections of AR-A014418 reduced immobility time in rats exposed to the forced swim test, which was a well-established model for antidepressant efficacy. Moreover, the specificity of this effect was supported by our finding that AR-A014418 decreased spontaneous as well as amphetamine-induced activity [2].

Clinical trial: currently no clinical data were available.

References:

- [1] Bhat R, Xue Y, Berg S, Hellberg S, Orm M, Nilsson Y, Rades ter AC, Jerning E, Markgren PO, Borgeg rd T, Nyl f M, Giménez-Cassina A, Hernández F, Lucas JJ, Díaz-Nido J, Avila J. Structural insights and biological effects of glycogen synthase kinase 3-specific inhibitor AR-A014418. J Biol Chem. 2003;278(46):45937-45.
- [2] Gould TD, Einat H, Bhat R, Manji HK. AR-A014418, a selective GSK-3 inhibitor, produces antidepressant-like effects in the forced swim test. Int J Neuropsychopharmacol. 2004;7(4):387-90.

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