MSI-1436

Cat. No.: HY-12219
CAS No.: 186139-09-3
Molecular Formula: C₃₇H₇₂N₄O₅S
Molecular Weight: 685.06
Target: Phosphatase
Pathway: Metabolic Enzyme/Protease
Storage: Powder
-20°C 3 years
4°C 2 years
In solvent
-80°C 6 months
-20°C 1 month
Solubility: 10 mM in DMSO

PREPARING STOCK SOLUTIONS

<table>
<thead>
<tr>
<th>Volume Concentration</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>1 mM</td>
<td>1.4597 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.2919 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1460 mL</td>
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</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description
MSI-1436 is a selective, non-competitive inhibitor of the enzyme protein tyrosine phosphatase 1B (PTB-1B), with an IC₅₀ of appr 1 µM, 200-fold preference over TC-PTP (IC₅₀, 224 µM).

IC₅₀ & Target
IC₅₀: 1 µM (PTB-1B), 224 µM (TC-PTP)[1]

In Vitro
In HepG2, MSI-1436 (10 µM, 30 min) alone has no effect on phosphorylation of IRβ, but in conjunction with 100 nM insulin, MSI-1436 increases p-IRβ 18-fold over untreated cells and by approximately threefold over cells treated with insulin alone. MSI-1436’s inhibition of TCPTP is approximately two logs less than the effect on PTP1B activity, with a resulting IC₅₀ value of 224 µM[1]. MSI-1436 (Trodsquemine, 10 µM) restores ERK phosphorylation in response to mGlur1/5 agonist DHPG in F11 neuronal cells. MSI-1436 (10 µM) rescues DHPG-induced holding currents and restores DSI in LMO4KO BLA neurons[2]. MSI-1436 (0.1-100 µM) blocks PTP1B activity, has insulin-mimetic effects in cultured neuronal cells[3].

In Vivo
MSI-1436 (10 mg/kg, i.p.) causes obesity-dependent body weight, reduces total body fat content and adipocyte size and lipid content of white adipose tissue of mice. MSI-1436 treatment significantly reduces plasma insulin levels. MSI-
MSI-1436 (10 mg/kg, i.p.) increases phosphorylation of STAT-3 2.7-fold and, in conjunction with 100 U/kg insulin, p-IRβ increases threefold over insulin alone-treated rats\[1\]. MSI-1436 (Trodusquemine) exhibits anxiolytic effect through a restoration of endocannabinoid (eCB) signaling within the amygdala\[2\]. MSI-1436 (5 mg/kg, i.p.) has an anti-diabetic effect on diabetic mice, and is sufficient to suppress food intake and cause weight loss in CD1 mice\[3\].

**PROTOCOL**

**Animal Administration** \[1\]

**Mice**

Male AKR/J mice are randomly placed on ad libitum 10, 45, or 60% fat kcal diets. After -14 weeks, mice are randomly assigned to three treatment groups (n=5-8 mice/group): MSI-1436 (initial dose of 10 mg/kg with three subsequent weekly doses of 5 mg/kg, intraperitoneally), vehicle (saline, 10 mL/kg, weekly 4×), or pair-fed (PF). PF animals are injected with saline (weekly 4×) and allotted the amount of food consumed daily by MSI-1436-treated animals. On day 23, mice are anesthetized and euthanized for blood and tissue collection, respectively. Plasma is obtained following centrifugation of blood 14,000 rpm for 10 min at 4°C.

**Rats**

Nine-week-old male Sprague-Dawley rats (225-260 g) with ad libitum access to normal rodent chow are dosed intraperitoneally with MSI-1436 (10 mg/kg, IP) or saline. After an overnight fast, the rats are dosed intraperitoneally with saline or 100 U/kg of insulin. At 30 min after dose, animals are killed, and hypothalami are harvested and homogenized in 1 mL of tissue extraction reagent plus phosphatase and protease inhibitors. Samples are centrifuged (14,000 rpm for 10 min at 4°C), and the protein content of the supernatants are quantitated via BCA kit.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**


Caution: Product has not been fully validated for medical applications. For research use only.

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