GSK2982772

Cat. No.: HY-101760
CAS No.: 1622848-92-3
Molecular Formula: C₂₀H₁₉N₅O₃
Molecular Weight: 377.4
Target: RIP kinase
Pathway: Apoptosis
Storage: Powder -20°C 3 years
         4°C  2 years
         In solvent -80°C 6 months
         -20°C 1 month

Solvent & Solubility

In Vitro DMSO : ≥ 100 mg/mL (264.97 mM)
* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Solvent</td>
<td>1 mM</td>
<td>5 mM</td>
<td>10 mM</td>
</tr>
<tr>
<td></td>
<td>Concentration</td>
<td></td>
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<tr>
<td></td>
<td>1 mM</td>
<td>2.6497 mL</td>
<td>13.2485 mL</td>
<td>26.4971 mL</td>
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<tr>
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<td>5 mM</td>
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<td>2.6497 mL</td>
<td>5.2994 mL</td>
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<tr>
<td></td>
<td>10 mM</td>
<td>0.2650 mL</td>
<td>1.3249 mL</td>
<td>2.6497 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description GSK2982772 is a potent and ATP competitive RIP1 inhibitor with an IC₅₀ of 16 nM.

IC₅₀ & Target IC₅₀: 16 nM (human RIP1 FP), 20 nM (monkey RIP1 FP), 2 μM (rat RIP1 FP), 2.5 μM (mouse RIP1 FP)[1]

In Vitro GSK2982772 shows more than 1,000-fold selectivity for ERK5 over a panel of over 339 kinases at 10 μM. In stimulated cellular systems, GSK2982772 is also able to reduce spontaneous production of cytokines (IL-1β and IL-6) in a concentration-dependent fashion from ulcerative colitis explant tissue in overnight incubations. GSK2982772 produces a weak concentration-dependent inhibition of hERG in human embryonic kidney (HEK-293) cells, with an estimated IC₅₀ of 195 μM, and also shows a weak activation of the human Pregnane X receptor (hPXR) with an EC₅₀ of 13 μM[1].

In Vivo GSK2982772 is dosed orally 15 min prior to TNF and shows 68, 80, and 87% protection from temperature loss over 6 h, at doses of 3, 10, and 50 mg/kg, respectively. In the corresponding TNF/zVAD model, GSK2982772 shows 13, 63,
and 93% protection from temperature loss over 3 h. GSK2982772 displays a good free fraction in blood in rats (4.2%),
dogs (11%), cynomolgus monkeys (11%), and humans (7.4%). The inhibitor has a good pharmacokinetic profile across
both rats and monkeys. GSK2982772 distributes into a range of tissues including the colon, liver, kidney, and heart at
concentrations comparable to those of blood. However, GSK2982772 has low brain penetration in rat (4%) despite
possessing good cell permeability ($21 \times 10^{-6}$ cm/s)$^{[1]}$.

**PROTOCOL**

**Animal Administration** $^{[1]}$

Mice: A total of 7 mice per dose group are orally predosed with saline or GSK2982772 at doses of 3, 10, and 50
mg/kg 15 min before i.v. administration of mouse TNF (30 μg/mouse). Temperature loss in the mice is measured by
a rectal probe. The study is terminated after 6 h when the control group lost 7 °C$^{[1]}$.

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

**REFERENCES**

$^{[1]}$. Harris PA, et al. Discovery of a First-in-Class Receptor Interacting Protein 1 (RIP1) Kinase Specific Clinical Candidate (GSK2982772) for the Treatment of

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

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