Product Data Sheet

Chemical Properties

Product Name: Tankyrase Inhibitors (TNKS) 22
Cas No.: M.Wt: 475.56
Formula: C25H25N5O3S
Synonyms: TNKS 22; TNKS22; TNKS-22
Chemical Name: 3-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)-N-((1r,4r)-4-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclohexyl)propanamide
Canonical SMILES: O=C1NC(SCC(N[C@H]2CC[C@H](C3=NN=C(C4=CC=CC=C4)O3)CC2)=O)=NC5=CC=CC=C51
Solubility: <4.76mg/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.
Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: Chromatin/Epigenetics
Pathways: PARP
Description:
Tankyrase Inhibitors (TNKS) 22 is a potent, selective and orally bioavailable inhibitor of tankyrase with IC50 value of 0.1nM [1].
Tankyrase 1 and tankyrase 2 are members of PARP family. They can use NAD+ as substrates to transfer ADP-ribose polymers onto target proteins. The tankyrase are found to bind to PARSylate axin proteins which are the negative regulator of Wnt pathway. It makes tankyrase to be targets
in treatment for adenomatous polyposis coli. Tankyrase inhibitors 22 is an optimization of the previous hit compound inhibitor 8 with improved potency and selectivity. It has excellent effects in both tankyrase assay and cellular assay (total β-catenin degradation assay in SW480 cells) with IC50 values of 0.1nM and 3.7nM, respectively. In addition, it is found to be a dual binder with both the nicotinamide pocket and the induced pocket of the enzymes [1].

In the in vivo studies in rodents, tankyrase inhibitors 22 is found to potently inhibit TNKS2 autoparsylation with IC50 value of 4.1nM. It also causes stabilization and accumulation of axin protein in SW480 cells with EC50 value of 3.9nM. In DLD-1 cells with truncated APC, the inhibitor inhibits the STF reporter transcription with IC50 value of 0.6nM suggesting its downstream inhibitory activity on Wnt-associated transcription [1].

Reference:

Protocol

Cell experiment:

<table>
<thead>
<tr>
<th>Cell lines</th>
<th>SW480-TBC cell lines</th>
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</thead>
<tbody>
<tr>
<td>Preparation method</td>
<td>The solubility of this compound in DMSO is &gt;10 mM. 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.</td>
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<tr>
<td>Reacting conditions</td>
<td>24 h; IC50=3.7nM</td>
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<tr>
<td>Applications</td>
<td>Tankyrase Inhibitors (TNKS) 22, lead-optimized phenyloxadiazole compounds, has a good enzymatic potency and cellular potency with IC50 value of 3.7 nM in the SW480-TBC cellular assay. The compound demonstrated excellent potencies in TNKS2 autoparsylation assay and the two additional functional cellular assays.</td>
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</table>

Animal experiment [3]:

<table>
<thead>
<tr>
<th>Animal models</th>
<th>Athymic nude mice.</th>
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<tbody>
<tr>
<td>Dosage form</td>
<td>10 and 50 mg/kg; q.d.; oral taken</td>
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<tr>
<td>Applications</td>
<td>Tankyrase Inhibitors (TNKS) 22 was evaluated for Wnt-pathway specific pharmacological activity in mouse tumor pharmacodynamic (PD) models. Upon once daily oral administration (at 10 and 50</td>
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</table>
mg/kg) to mice (n=4) bearing human DLD-1 tumors for 3 days, both compounds exhibited statistically significant, dose-dependent axin2 accumulation (2.7-to 3.5-fold) and inhibition of STF (51–58%) at day 3 (24 h after the last dose).

**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.

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**Reference:**


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**Caution**

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short-term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.