Salirasib

Cat. No.: HY-14754
CAS No.: 162520-00-5
Molecular Formula: C₉₂H₃₀O₂S
Molecular Weight: 358.54
Target: Ras; Autophagy
Pathway: GPCR/G Protein; Autophagy
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: ≥ 50 mg/mL (139.45 mM)
H₂O: < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.7891 mL</td>
<td>13.9454 mL</td>
<td>27.8909 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5578 mL</td>
<td>2.7891 mL</td>
<td>5.5782 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2789 mL</td>
<td>1.3945 mL</td>
<td>2.7891 mL</td>
</tr>
</tbody>
</table>

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

In Vivo
1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.97 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.97 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.97 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Salirasib is a Ras inhibitor that inhibits specifically both oncogenically activated Ras and growth factor receptor-mediated Ras activation, resulting in the inhibition of Ras-dependent tumor growth.

IC₅₀ & Target
Ki: 2.6 μM (PPMTase)
### In Vitro

Salirasib (12.5-100 μM) inhibits the proliferation of ELT3 cells in a dose-dependent manner with an average IC$_{50}$ of 58.57±4.59 μM. The effects of Salirasib on the TSC2-null cells are evidently mimicked by DN-Rheb but not by DN-Ras. Salirasib reduces Rheb in TSC2-null cells and TSC2 expression rescues the cells from the inhibitory effect of Salirasib. Salirasib reduces phosphorylation of S6K but not of ERK in the TSC2-null ELT3 cells$^1$. Salirasib (50, 100, 150 μM) induces a dose- and time-dependent decrease of cell growth in HCC cells. Salirasib reduces cell proliferation through modulation of cell cycle effectors and inhibitors. Salirasib induces apoptosis in HepG2 and Hep3B cells. The growth inhibitory effect of salirasib in HCC cell lines is associated with mTOR inhibition independent of ERK or Akt activation$^2$.

### In Vivo

Salirasib (40, 60 or 80 mg/kg, p.o.) significantly inhibits the tumor growth in a dose dependent manner in vivo$^1$. Salirasib (5 mg/kg, i.p.) significantly decreases Ras expression in the dy$^{2J}$/dy$^{2J}$ mice, and causes an increase in Ras expression which is by far much lower than the increase observed in the dy$^{2J}$/dy$^{2J}$ mice. Salirasib treatment is associated with significantly inhibition of both MMP-2 and MMP-9 activities in the dy$^{2J}$/dy$^{2J}$ mice$^2$. Salirasib (10 mg/kg, i.p.) inhibits tumour growth in a subcutaneous xenograft mice model without weight loss$^3$.

### PROTOCOL

#### Cell Assay$^3$

For time dependent response studies, cells are harvested with 0.05% Trypsin-EDTA daily for 1 to 7 days and counted under the microscope using the Trypan blue exclusion method. For dose response studies, cells are incubated in medium supplemented with salirasib or DMSO for 3 days. Cell viability is determined using a colorimetric WST-1 assay according to the manufacturer's instructions. The IC$_{50}$ value, at which 50% of the cell growth is inhibited compared with DMSO control, is calculated by nonlinear regression analysis using GraphPad Prism software.

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

#### Animal Administration$^3$

Six week old female athymic NMRI nu/nu mice are housed in filter-topped cages and receive food and water ad libitum. Tumors are generated by subcutaneous injection into the right lower flank with $5\times10^6$ HepG2 cells suspended in 100 μL PBS in 12 mice. Two weeks after cell inoculation, when palpable tumours are established, mice are separated into salirasib-treated (n=6) and control group (n=4). Two animals do not develop tumours at that time point and had to be excluded from the study. They receive daily i.p. injections of 10 mg/kg salirasib or a similar volume of vehicle solution (PBS containing 2.5% v/v ethanol, pH 8.0) for 12 days. Tumor dimensions are recorded three times per week with a digital calliper starting with the first day of treatment. Tumor volumes are estimated as follows: $V$ (mm$^3$)=$\frac{(\text{length}\times\text{width}^2)}{2}$. Tumour weights are recorded at the time of sacrifice in order to evaluate treatment response.

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

### CUSTOMER VALIDATION

- Int J Pharm. 2019 Nov 9;118823.

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### REFERENCES


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