**SN-38**

Cat. No.: HY-13704  
CAS No.: 86639-52-3  
Molecular Formula: $C_{22}H_{20}N_2O_5$  
Molecular Weight: 392.4  
Target: Topoisomerase; Autophagy  
Pathway: Cell Cycle/DNA Damage; Autophagy  
Storage:  
- Powder: $-20^\circ C$ 3 years  
- $4^\circ C$: 2 years  
- In solvent: $-80^\circ C$ 6 months  
- $-20^\circ C$: 1 month

**Solvent & Solubility**

In Vitro  
DMSO: $\geq 40$ mg/mL (101.94 mM)  
*“$\geq$” means soluble, but saturation unknown.*

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.5484 mL</td>
<td>12.7421 mL</td>
<td>25.4842 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.5097 mL</td>
<td>2.5484 mL</td>
<td>5.0968 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2548 mL</td>
<td>1.2742 mL</td>
<td>2.5484 mL</td>
</tr>
</tbody>
</table>

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

**BIOLOGICAL ACTIVITY**

**Description**  
SN-38 (NK012) is an active metabolite of the Topoisomerase I inhibitor Irinotecan. SN-38 (NK012) inhibits DNA and RNA synthesis with IC$_{50}$s of 0.077 and 1.3 μM, respectively.

**IC$_{50}$ & Target**  
Topoisomerase I

**In Vitro**  
The IC$_{50}$ values for LoVo, HCT116, and HT29 cell lines is 20 nM, 50 nM, 130 nM, respectively. In all three SN-38 (NK012) resistant cell lines Top1 activity is maintained in the presence of high concentrations of SN-38$^{[2]}$.

**In Vivo**  
SN-38 (NK012), the active and toxic metabolite of the anticancer prodrug Irinotecan. At 30 minutes after administration, Irinotecan plasma concentrations in Scl0a/1b$^{(-/-)}$ mice are 1.9-fold higher than in the wild-type mice (1.89 vs. 1.01 μM, respectively), whereas SN-38 (NK012) plasma concentrations of Scl0a/1b$^{(-/-)}$ mice are 8-fold higher compare with wild-type mice (0.4 μg/mL vs. 0.05 μg/mL, respectively). Overall plasma exposure [AUC$_{5-240}$] of Irinotecan is 1.7-fold higher in Oatp1a/1b knockout mice versus wild-type mice (209.8±6.7 vs. 120.9±4.4 μg·h/mL).
M/min; P<0.01), and 2.9-fold higher for SN-38 (50±2.9 vs. 12±2 μM/min; P<0.001)[3].

**PROTOCOL**

**Cell Assay**[2]

In vitro SN-38 (NK012) sensitivity is determined using the MTT assay. Cells are seeded in 96-well plates, and a range of SN-38 (NK012) concentrations is added the following day. Following 48 h of drug exposure, the medium is discarded and the plates are incubated with medium containing MTT (0.5 mg/mL) for 3 h. Acidified (0.02 M HCl) sodium dodecyl sulphate (20 %) is added to dissolve the formed formazan. Optical density at 570 nm (and 670 nm for background) is measured, and the cell viability is calculated in percent compared to untreated cells. Experiments are repeated three times and the mean IC₅₀ value ± standard deviation is determined. Relative resistance for each resistant cell line is calculated by dividing the mean IC₅₀ value of the resistant cell line by the mean IC₅₀ value of the corresponding parental cell line[2].

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

**Animal Administration**[3]

Female wild-type, Slco1a/1b(−/−)(Oatp1a/1b knockout), Slco1a/1b(−/−);1B1(tg), and Slco1a/1b(−/−);1B3(tg) (liver-specific OATP1B1 and OATP1B3 humanized transgenic) mice of comparable genetic background (>99% FVB) between 8 and 14 weeks of age are used. Irinotecan (20 mg/mL in water-based solution containing NaOH, lactic acid, and sorbitol) is diluted with saline (to 2 mg/mL) for administration of 10 mg/kg; 5 μL/g bodyweight are administered intravenously to mice. SN-38 (NK012) is dissolved in DMSO (1 mg/mL) and 1 μL/g body weight is administered intravenously to mice to achieve a dosage of 1 mg/kg. The experiments are terminated by isoflurane anaesthesia, heparin-blood sampling by cardiac puncture followed by cervical dislocation and tissue collection. Blood samples are centrifuged at 5,200 × g for 5 minutes at 4°C and plasma is collected and stored at −30°C until analysis.

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**REFERENCES**

