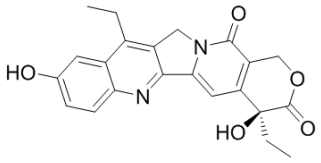
SN-38

Cat. No.:	HY-13704
CAS No.:	86639-52-3
Molecular Formula:	$C_{22}H_{20}N_2O_5$
Molecular Weight:	392.4
Target:	Topoisomerase; ADC Cytotoxin; Autophagy
Pathway:	Cell Cycle/DNA Damage; Antibody-drug Conjugate/ADC Related; 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 : 25 mg/mL (**63.71 mM;** Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5484 mL	12.7421 mL	25.4842 mL
	5 mM	0.5097 mL	2.5484 mL	5.0968 mL
	10 mM	0.2548 mL	1.2742 mL	2.5484 mL

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 Slco1a/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 Slco1a/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 μ

	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 IC_{50} value ± standard deviation is determined. Relative resistance for each resistant cell line is calculated by dividing the mean IC_{50} value of the resistant cell line by the mean IC_{50} 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]	Mice[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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **J Mol Med (Berl)**. 2019 Jun 14.
- **Int J Pharm**. 2019 Aug 1:118588.
- **Life Sci**. 2019 Jun 4. pii: S0024-3205(19)30441-2.

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REFERENCES

[1]. Wallin A, et al. Anticancer effect of SN-38 on colon cancer cell lines with different metastatic potential. Oncol Rep. 2008 Jun;19(6):1493-8.

[2]. Jensen NF, et al. Characterization of DNA topoisomerase I in three SN-38 resistant human colon cancer cell lines reveals a newpair of resistance-associated mutations. J Exp Clin Cancer Res. 2016 Mar 31;35:56.

[3]. Stewart CF, et al. Disposition of irinotecan and SN-38 following oral and intravenous irinotecan dosing in mice. Cancer Chemother Pharmacol. 1997;40(3):259-65.

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

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