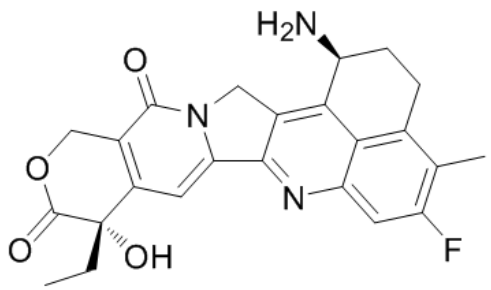
Product Data Sheet

Product Name: Exatecan (DX-8951)
Cat. No.: GC33108

Chemical Properties

Cas. No.	171335-80-1		
SMILES	O=C1[C@](O)(CC)C2=C(CO1)C(N3CC4=C5C6=C(CC[C@@H]5N)C(C)=C(F)C=C6N=C4C3=C2)=O		
Formula	$C_{24}H_{22}FN_3O_4$	M.Wt	435.45
Solubility	Soluble in DMSO	Storage	Store at -20°C,protect from light
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.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Product Data Sheet

Protocol

Cell experiment [1]:

Cell lines	32 malignant cell lines
Preparation Method	Thus 500-20,000 cells/well in 150 u1 of medium were plated in 96-well flat-bottomed microplates and grown for 24h (P388, CCRF-CEM and K562 cells for 4h), the Exatecan (DX-8951) (in 50 µl medium/well), or the medium alone as a control was added, and the cells were cultured for an additional 3 days. Then calculated Growth inhibition of 50% (GI50) .
Reaction Conditions	Different concentrations for 24 h
Applications	Exatecan (DX-8951) showed strong antiproliferating activity,and the mean GI50 values against breast cancers colon cancers, stomach cancers, and lung cancers were 2.02 ng/ml, 2.92 ng/ml, 1.53 ng/ml, and 0.877 ng/ml respectively.

Animal experiment [2]:

Animal models	Male 6-week-old BALB/c-nu/nu nude mice
Preparation Method	The human tumor lines inoculated s.c. into nude mice and maintained as solid tumors. Various human tumors maintained in nude mice were excised and
Dosage form	50 mg/kg, i.v.

Product Data Sheet

Applications	The q4d×4 schedule more readily caused the regressive effects of Exatecan (DX-8951) compared with the q7d×3, and a schedule of q4d×3 more frequently permitted regrowth of tumors than did the q4d×4 schedule.

References:
[1]: Mitsui I, Kumazawa E, Hirota Y, Aonuma M, Sugimori M, Ohsuki S, Uoto K, Ejima A, Terasawa H, Sato K. A new water-soluble camptothecin derivative, DX-8951f, exhibits potent antitumor activity against human tumors in vitro and in vivo. Japanese journal of cancer research. 1995 Aug;86(8):776-82.
[2]:Kumazawa E, Jimbo T, Ochi Y, et al. Potent and broad antitumor effects of DX-8951f, a water-soluble camptothecin derivative, against various human tumors xenografted in nude mice[J]. Cancer chemotherapy and pharmacology, 1998, 42(3): 210-220.

Background

Exatecan (DX-8951) is a nonprodrug camptothecin (CPT) derivative, exhibits significant topoisomerase I inhibition [1]. Exatecan (DX-8951) inhibited topoisomerase I with IC50 of 2.2 μM (0.975 μg/ml) [2].

Exatecan (DX-8951) and SN-38 inhibited topoisomerase activity with IC50 values of 0.82 and 2.3 μg/mL, respectively, topoisomerase I was obtained from SUIT-2 cells [3]. Exatecan (DX-8951)(20 ng/ml) induced DNA fragmentation. In an extract from treated SUIT-2 cells, about 60% of DNA was fragmented at the Exatecan (DX-8951) concentration of 20 ng/ml. Exatecan (DX-8951)(0.05 μg/ml, 24 h) induced the specific features of apoptosis, namely chromatin condensation, nuclear fragmentation and cytoplasmic vacuolation were apparent in SUIT-2 cells [3].

Exatecan (DX-8951) has shown activity in vivo against a wide range of human tumor xenografts in nude mice, including gastric, pancreatic, colon, breast, ovary, and lung tumors [4]. Exatecan (DX-8951) suppressed the growth of human gastric adenocarcinoma SC-6 xenografted into nude mice. When mice were treated i.v. with Exatecan (DX-8951) three times at 4-day intervals, significant inhibition of tumor growth was observed over a wide dose range (3.325 mg/kg to 50 mg/kg of total dose) without toxic death. Its antitumor activity was dependent on the total dose, and at the highest

dose of 50 mg/kg, the tumor growth inhibition rate was 92% [2].

References:

[1]. Kumazawa E, Jimbo T, Ochi Y, et al. Potent and broad antitumor effects of DX-8951f, a water-soluble camptothecin derivative, against various human tumors xenografted in nude mice[J]. Cancer chemotherapy and pharmacology, 1998, 42(3): 210-220.
[2]. Mitsui I, Kumazawa E, Hirota Y, Aonuma M, Sugimori M, Ohsuki S, Uoto K, Ejima A, Terasawa H, Sato K. A new water-soluble camptothecin derivative, DX-8951f, exhibits potent antitumor activity against human tumors in vitro and in vivo. Japanese journal of cancer research. 1995 Aug;86(8):776-82.
[3]. Takiguchi S, Kumazawa E, Shimazoe T, Tohgo A, Kono A. Antitumor effect of DX-8951, a novel camptothecin analog, on human pancreatic tumor cells and their CPT-11-resistant variants cultured in vitro and xenografted into nude mice. Japanese journal of cancer research. 1997 Aug;88(8):760-9.
[4]. De Jager R, Cheverton P, Tamanoi K, et al. DX-8951f: summary of Phase I clinical trials[J]. Annals of the New York Academy of Sciences, 2000, 922(1): 260-273.

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