

Product Data Sheet

Product Name: Topotecan HCl

Cat. No.: GC13359

Chemical Properties

Cas. No. 119413-54-6

Chemical Name (S)-10-((dimethylamino)methyl)-4-ethyl-4,9-dihydroxy-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione hydrochloride

SMILES Cl[H].O=C1N(C([H])([H])C2=C([H])C(C(C([H])([H])N(C([H])([H])[H])C([H])([H])[H])=C3O[H])=C(C([H])=C3[H])N=C42)C4=C([H])C([C@@](C([H])([H])C([H])([H])[H])5O[H])=C1C([H])([H])OC5=O

Formula C₂₃H₂₄ClN₃O₅

M.Wt 457.91

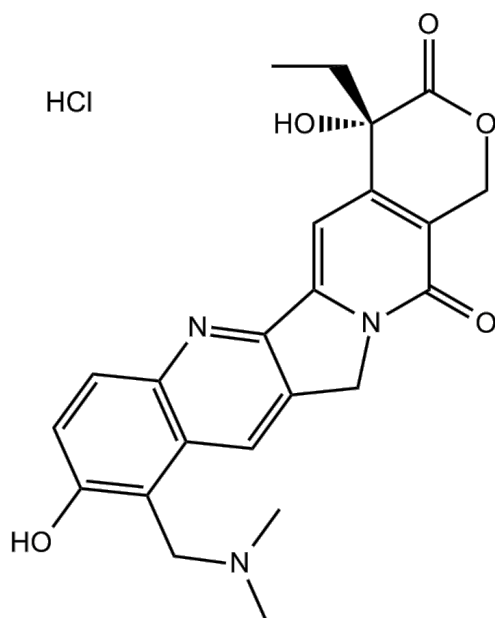
Solubility ≥ 22.9mg/mL in DMSO

Storage 4°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



Protocol

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

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Cell experiment [1]:

Cell lines U251, U87, GSCs-U251, GSCs-U87 cells

U251, U87, GSCs-U251 and GSCs-U87 cells were treated with different Preparation Method concentrations of Topotecan HCl for 24h, and cell viability were assayed by CCK-8.

Reaction Conditions 0.02, 0.2, 2, 20, 40μM ; 24h

Applications The cell viability was inhibited by Topotecan HCl in a dose-dependent manner. The IC₅₀ values of Topotecan HCl at 24h were 2.73±0.25μM of U251 cells, 2.95±0.23μM of U87 cells, 5.46±0.41μM of GSCs-U251 and 5.95±0.24μM of GSCs-U87.

Animal experiment [2]:

Animal models Nonobese diabetic/severe combined immune deficient (NOD/SCID) mice bearing SK-N-BE(2)

Preparation Method When tumors reached 0.5cm in diameter, the animals were randomized into 4 groups and treated daily by oral gavage. The animals were grouped as: Control group, Topotecan HCl group (1.0mg/kg), Pazopanib group (150mg/kg) and Topotecan HCl+Pazopanib group (1.0mg/kg+150mg/kg). Drugs were administered daily over a period of 56 days. The animals belonging to the Topotecan HCl+Pazopanib group, which remained alive, were also retreated from the 103rd day to evaluate the impact of resuming treatment on reversing drug resistance. Retreatment was continued until the 125th day, after which the mice were sacrificed.

Dosage form 1.0mg/kg/d; 56 or 56+23d; p.o.

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Applications Compared with control, both the single agents significantly enhanced survival of animals. The survival in Topotecan HCl+Pazopanib group was significantly higher compared with both control

References:

- [1] Zhang FL, Wang P, Liu YH, et al. Topoisomerase I inhibitors, shikonin and Topotecan HCl, inhibit growth and induce apoptosis of glioma cells and glioma stem cells. PLoS One. 2013;8(11):e81815.
- [2] Kumar S, Mokhtari RB, Sheikh R, et al. Metronomic oral Topotecan HCl with pazopanib is an active antiangiogenic regimen in mouse models of aggressive pediatric solid tumor. Clin Cancer Res. 2011;17(17):5656-5667.

Background

Topotecan HCl is a topoisomerase I inhibitor that acts as a Topo I poison. Topotecan HCl specifically targets the topoisomerase I–DNA cleavage complex, acting after DNA cleavage and inhibiting the re-ligation step. Topotecan HCl can cross the blood–brain barrier and exhibits cytotoxicity against a variety of tumor cell types, showing significant activity in the treatment of brain tumors^[1].

In vitro, Topotecan HCl (0.02-40 μ M; 12-48h) dose- and time-dependently inhibited the proliferation of U251, U87, GSCs-U251, and GSCs-U87 cells, with IC₅₀ values at 24h of 2.73 $\pm$ 0.25, 2.95 $\pm$ 0.23, 5.46 $\pm$ 0.41, and 5.95 $\pm$ 0.24 μ M, respectively^[1]. Topotecan HCl (3 μ M; 24h) significantly upregulated p21 protein levels and induced cell cycle arrest at the G0/G1 and S phases in U251, U87, GSCs-U251, and GSCs-U87 cells^[1]. Topotecan HCl (0.1-1000ng/mL; 72h) caused a dose-dependent reduction in the viability of HUVECs, with an IC₅₀ of 4.87ng/mL^[2]. Among neuroblastoma cell lines, the IC₅₀ values of Topotecan HCl on SH-SY5Y, BE(2)-c and SK-N-BE(2) were 5.3ng/mL, 45.6ng/mL and 65.0ng/mL, respectively. Among sarcoma cell lines, the IC₅₀ values of Topotecan HCl on RH30, RD, and KHOS cell lines were 7.4ng/mL, 7.5ng/mL, and 4.9ng/mL, respectively^[2].

In vivo, Topotecan HCl (1mg/kg/d; p.o.; 56d) significantly improved the survival of nonobese diabetic/severe combined immune deficient (NOD/SCID) mice bearing SK-N-BE (2)^[2]. In IGROV-1 tumour-bearing mice, Topotecan HCl (10mg/kg) given intraperitoneally every 4 days for four occasions markedly increased survival time over control mice^[3].

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- [2] Kumar S, Mokhtari RB, Sheikh R, et al. Metronomic oral Topotecan HCl with pazopanib is an active antiangiogenic regimen in mouse models of aggressive pediatric solid tumor. Clin Cancer Res. 2011;17(17):5656-5667.
- [3] Pratesi G, Tortoreto M, Corti C, Giardini R, Zunino F. Successful local regional therapy with Topotecan HCl of intraperitoneally growing human ovarian carcinoma xenografts. Br J Cancer. 1995;71(3):525-528.

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