Intoplicine

Cat. No.: HY-101647

CAS No.: 125974-72-3

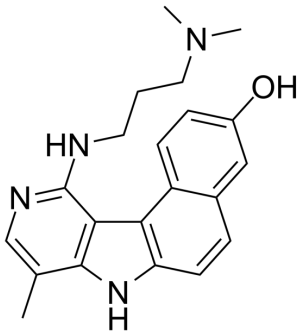
Molecular Formula: $C_{21}H_{24}N_4O$

Molecular Weight: 348.44

Target: Topoisomerase

Pathway: Cell Cycle/DNA Damage

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 80 mg/mL (229.59 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8699 mL	14.3497 mL	28.6993 mL
	5 mM	0.5740 mL	2.8699 mL	5.7399 mL
	10 mM	0.2870 mL	1.4350 mL	2.8699 mL

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 mg/mL (5.74 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2 mg/mL (5.74 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2 mg/mL (5.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Intoplicine (RP 60475), an antitumor derivative in the 7H-benzo[e]pyrido[4,3-b]indole series, is a DNA topoisomerase I and II inhibitor. Intoplicine strongly binds DNA ($K_A = 2 \times 10^5$ /M) and thereby increases the length of linear DNA[1][2].

IC_{50} & Target	Topoisomerase I	Topoisomerase II

In Vitro

With 1-hour exposure to Intoplicine at final concentrations of 2.5 micrograms/mL and 10.0 micrograms/mL, 26% and 54% of the assessable specimens shows positive in vitro responses, respectively[2].
With continuous exposure to Intoplicine at concentrations of 0.25 micrograms/mL and 2.5 micrograms/mL, 16% and 71% of

	the assessable specimens showed positive responses, respectively[2]. Activity is seen against breast (71%), non-small-cell lung (69%), and ovarian (45%) cancer colony-forming units at a Intoplicine concentration of 10.0 micrograms/mL after 1-hour exposure[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	At the highest non-toxic dose (HNTD) (6 mg/kg/injection, total dose, 36 mg/kg), Intoplicine shows highly active with a T/C of 0% and a corresponding total log cell kill of 3[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	The assay is performed with various concentrations of calf thymus Topo II (20 to 0.1 decatenation units) in a 20 µL final reaction volume containing 0.25 µg of supercoiled pBR322 DNA, 20 mM Tris HC1 (pH 7.5), 60 mM KCl, 10 mM $MgCl_2$, 30 µg /mL bovine serum albumin, 0.5 mM EDTA, 0.5 mM Dithiothreitol, and 1 µM Intoplicine or water. The final nucleotide concentration is 20.8 µM.The reaction is assembled in ice and the reaction mixture is then incubated at 37°C for 5 min. Then sample is mixed at room temperature with 20 µL of preaggregated silver hydrosol and immediately analyzed by SERS. Control experiments consisting of measurement of the SERS spectra of buffer alone, Topo II alone, Intoplicine alone (1µM), DNA alone, Topo II+Intoplicine, and DNA+Intoplicine are performed under the same conditions, except that distilled water is used to adjust the reaction volume to 20µL[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	The K562 human erythroleukemia cell line is established from a patient with chronic myelogenous leukemia. Cells are in the exponential growth phase at 5-8×10^5 in RPMI 1640 (GIBCO) supplemented with 10% fetal calf serum (Seromed) and 2 mM L-glutamine. Cell growth and viability are determined by phase contrast microscopy and by using the trypan blue test. Cells (2×10^6) are incubated with 1 µM Intoplicine for 1 h at 37°C, washed twice with PBS by centrifugation (200× g at 4°C) and resuspended in 200 µL PBS[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Eckardt JR, et al. Activity of Intoplicine (RP60475), a new DNA topoisomerase I and II inhibitor, against human tumor colony-forming units in vitro. J Natl Cancer Inst. 1994 Jan 5;86(1):30-3.

[2]. Morjani H, et al. Molecular and cellular interactions between Intoplicine, DNA, and topoisomerase II studied by surface-enhanced Raman scattering spectroscopy. Cancer Res. 1993 Oct 15;53(20):4784-90.

[3]. Bissery MC, et al. Antitumor activity of intoplicine (RP 60475, NSC 645008), a new benzo-pyrido-indole: evaluation against solid tumors and leukemias in mice. Invest New Drugs. 1993;11(4):263-277.

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