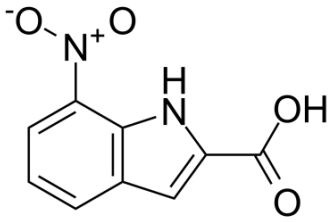
CRT0044876

Cat. No.:	HY-W014622
CAS No.:	6960-45-8
Molecular Formula:	$C_9H_6N_2O_4$
Molecular Weight:	206.15
Target:	DNA/RNA Synthesis
Pathway:	Cell Cycle/DNA Damage
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 : 50 mg/mL (242.54 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.8508 mL	24.2542 mL	48.5084 mL
	5 mM	0.9702 mL	4.8508 mL	9.7017 mL
	10 mM	0.4851 mL	2.4254 mL	4.8508 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: 2.5 mg/mL (12.13 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

CRT0044876 is a potent and selective apurinic/apyrimidinic endonuclease 1 (APE1) inhibitor (IC_{50}=~3 μM). CRT0044876 inhibits the AP endonuclease, 3′-phosphodiesterase and 3′-phosphatase activities of APE1, and is a specific inhibitor of the exonuclease III family of enzymes to which APE1 belongs. CRT0044876 potentiates the cytotoxicity of several DNA base-targeting compounds[1].

In Vitro

A key step in BER is the processing of an apurinic/apyrimidinic (AP) site intermediate by an AP endonuclease. CRT0044876 has an IC_{50} for inhibition of APE1 of ~3 μM and not only inhibits AP site cleavage catalyzed by purified APE1, but also cleavage directed by APE1 in a HeLa whole cell extract. CRT0044876 inhibits the 3′-phosphoglycolate diesterase activity of APE1 with an IC_{50} of ~5 μM[1].

CRT0044876 inhibits both the exonuclease and AP endonuclease activities of exonuclease III, but shows no inhibitory activity towards endonuclease IV. CRT0044876 has minimal effects on BamHI restriction endonuclease or topoisomerase I even at CRT0044876 concentrations of 100 μM[1].

At non-toxic concentrations, CRT0044876 potentiates the cytotoxicity of several DNA damaging agents, which generate damage that is repaired in the BER pathway, including some currently-used anticancer drugs. The combination of MMS and CRT0044876 leads to a synergistic increase in the level of AP sites. Consistent with CRT0044876 being a specific BER inhibitor, a strong potentiation of hmdUrd cytotoxicity is seen in CRT0044876-treated cells (HT1080 cells)[1].

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

REFERENCES

[1]. Madhusudan S, et al. Isolation of a small molecule inhibitor of DNA base excision repair. Nucleic Acids Res. 2005;33(15):4711-4724. Published 2005 Aug 19.

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