Tretazicar

Cat. No.: HY-13543

CAS No.: 21919-05-1

Molecular Formula: $C_9H_8N_4O_5$

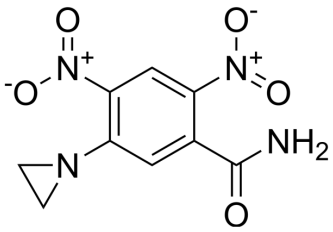
Molecular Weight: 252.18

Target: DNA Alkylator/Crosslinker

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (495.68 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.9654 mL	19.8271 mL	39.6542 mL
	5 mM	0.7931 mL	3.9654 mL	7.9308 mL
	10 mM	0.3965 mL	1.9827 mL	3.9654 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: ≥ 2.08 mg/mL (8.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (8.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tretazicar (CB 1954), an antitumor proagent, is highly selective against the Walker 256 rat tumour line. Tretazicar is enzymatically activated to generate a bifunctional agent, which can form DNA-DNA interstrand cross-links. Tretazicar in rat cells involves the reduction of its 4-nitro group to a 4-hydroxylamine by the enzyme NAD(P)H:quinone oxidoreductase 1 (NQO1)[1][2].

In Vitro

Tretazicar (CB 1954) (0.1-1000 μM; 3 days) has sensitivity for retrovirally transduced AB22 (AB22-nr) cells with an IC_{50} of 3 μM [3].

DNA cross-link formation in affected cells is a result of the bioactivation of the drug by the enzyme DT diaphorase (NAD(P)H dehydro-genase (quinone)) in the Walker cells which reduces the 4-nitro group of Tretazicar. The product of this reaction is a difunctional alkylating agent, 5-aziridin-1-yl-4-hydroxylamino-2-nitrobenzamide[4].

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

In Vivo

Tretazicar (CB 1954) (80 mg/kg; i.p. on days 2 and 9) results in a significant increase in survival[3].

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Animal Model:	Female BALB/c mice (AB22-nr, SKOV3 human ovarian tumour xenograft)[3]
Dosage:	80 mg/kg
Administration:	i.p. on days 2 and 9
Result:	The median survival of the AB22-nr was 49 days. Resulted in a significant increase in survival.

REFERENCES

[1]. Knox RJ,et al. Bioactivation of 5-(aziridin-1-yl)-2,4-dinitrobenzamide (CB 1954) by human NAD(P)H quinone oxidoreductase 2: a novel co-substrate-mediated antitumor prodrug therapy. Cancer Res. 2000 Aug 1;60(15):4179-86.

[2]. Knox RJ, et al. CB 1954: from the Walker tumor to NQO2 and VDEPT. Curr Pharm Des. 2003;9(26):2091-104.

[3]. Green NK, et al. Immune enhancement of nitroreductase-induced cytotoxicity: studies using a bicistronicadenovirus vector. Int J Cancer. 2003 Mar 10;104(1):104-12.

[4]. Drabek D, et al. The expression of bacterial nitroreductase in transgenic mice results in specific cell killing by the prodrug CB1954. Gene Ther. 1997 Feb;4(2):93-100.

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