上海源叶生物科技有限公司
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产品名称：Tretazicar
CAS 号：21919-05-1
产品货号：S89139

生物活性：

Description

Tretazicar (CB 1954) 是一种抗肿瘤前体，对 Walker 256 大鼠肿瘤细胞系具有很高的效力和选择性。Tretazicar 酶促活化后生成双功能试剂，该试剂可以形成 DNA-DNA 链间交联。大鼠细胞中的 Tretazicar 涉及通过酶 NAD(P)H：醌氧化还原酶 1 (NQO1) 将其 4-硝基还原为 4-羟基胺。

Cellular Effect

Cell Line	Type	Value	Description
CHO-AA8	IC_{50}	560 µM	Growth inhibition of aerobic chinese hamster ovary fibroblast AA8 cell line using an exposure time of 18 hours
CHO-AA8	IC_{50}	563 µM	Aerobic cytotoxicity was assessed in a growth inhibition assay using log phase cultures of the chinese hamster ovary fibroblast line AA8
EMT6	IC_{50}	0.098 µM	Growth inhibitory potency against NTR-Transfected (nitroreductase) mouse mammary cell line known as EMT6-NTRpuro cell line
EMT6	IC_{50}	0.098 µM	Antiproliferative activity against mouse EMT6 NTRpuro cells after 18 hrs
EMT6	IC_{50}	71 µM	Inhibitory activity against EMT6 (mouse mammary carcinoma) murine cell line
EMT6	IC_{50}	83 µM	Antiproliferative activity against mouse wild type EMT6 NTR-ve cells after 18 hrs
Mammary carcinoma cell line	IC_{50}	710000 nM	Cytotoxicity in non-NTR-expressing mouse mammary carcinoma cell line (EMT6).
Ovarian cancer cell line	IC_{50}	174000 nM	Cytotoxicity in non-NTR-expressing human ovarian carcinoma cell line (SKOV).
PC-3	IC_{50}	1.792 nM	Cytotoxicity against human PC3 cells assessed as reduction in cell viability measured after 48 hrs in presence of Staphylococcus saprophyticus nitroreductase and NADH by SRB assay
PC-3	IC_{50}	1.792 nM	Cytotoxicity against human PC3 cells expressing Staphylococcus saprophyticus nitroreductase NtrB assessed as reduction in cell viability in presence of NADH as cofactor after 48 hrs by SRB assay
RT-112	IC_{50}	0.15 µM	Cytotoxicity against NQO2 expressing human RT112 cells in presence of NRH cofactor by MTT assay
RT-112	IC_{50}	88.75 µM	Cytotoxicity against NQO2 expressing human RT112 cells by MTT assay
SK-OV-3	IC_{50}	0.64 µM	Growth inhibitory potency against NTR-Transfected (nitroreductase) human ovarian cell line known as SKOV3-NTR neo cell line

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	SK-OV-3	IC_{50}	0.76 μM	In vitro for cytotoxicity against SKOV-3 cells in the presence of 1 mM NADH co-factor
	SK-OV-3	IC_{50}	1.01 μM	In vitro for cytotoxicity against SKOV-3 cells in the presence of 1 mM NADH co-factor and 1 ug/mL Escherichia coli B nitroreductase (NTR)
	SK-OV-3	IC_{50}	174 μM	Inhibitory activity against SKOV3 (human ovarian carcinoma) cell line in human
	SK-OV-3	IC_{50}	182 μM	In vitro for cytotoxicity against SKOV-3 cells in the absence of co-factor
	SK-OV-3	IC_{50}	2 μM	Antiproliferative activity against NTR expressing human SKOV3 cells after 18 hrs
	SK-OV-3	IC_{50}	4.7 μM	Inhibitory activity against SKOV3 (human ovarian carcinoma) cell line with Escherichia coli nitroreductase combination after 18 hours drug exposure
	SK-OV-3	IC_{50}	4.7 μM	Antiproliferative activity against NTR expressing human SKOV3 cells infected with 100 pfu/cell retrovirus after 18 hrs
	SK-OV-3	IC_{50}	52 μM	Inhibitory activity against SKOV3 (human ovarian carcinoma) cell line infected at lower infection rate of 10 pfu/cell with Escherichia coli nitroreductase combination after 18 hours drug exposure
	SK-OV-3	IC_{50}	52 μM	Antiproliferative activity against NTR expressing human SKOV3 cells infected with 10 pfu/cell retrovirus after 18 hrs
	SK-OV-3	IC_{50}	625 μM	Antiproliferative activity against human SKOV3 cells infected with 10 pfu/cell retrovirus after 18 hrs
	SK-OV-3	IC_{50}	> 1000 μM	Inhibitory activity against SKOV3 (human ovarian carcinoma) cell line without Escherichia coli nitroreductase combination after 18 hours drug exposure
	SK-OV-3	IC_{50}	> 1000 μM	Antiproliferative activity against human SKOV3 cells infected with 100 pfu/cell retrovirus after 18 hrs
	SK-OV-3	IC_{50}	> 625 μM	Inhibitory activity against SKOV3 (human ovarian carcinoma) cell line without Escherichia coli nitroreductase combination after 18 hours drug exposure
	SK-OV-3	IC_{50}	> 790 μM	Antiproliferative activity against human SKOV3 cells after 18 hrs
	T78-1	IC_{50}	158 μM	Cytotoxicity in T78-1 (NR-negative) cell lines
	T78-1	IC_{50}	395 μM	In vitro cytotoxicity against Chinese hamster V79-derived cell line T78-1 transfected with Escherichia coli B nitroreductase (NTR)
	UV4	IC_{50}	11.7 μM	Growth inhibition of aerobic chinese hamster ovary fibroblast UV4 cells using an exposure time of 18 hours
	V79	IC_{50}	0.036 μM	Inhibitory activity against V79 (chinese hamster fibroblast) cell line with Escherichia coli nitroreductase combination

			after 72 hours drug exposure
V79	IC_{50}	0.036 μM	Antiproliferative activity against NTR expressing chinese hamster V79 cells after 72 hrs
V79	IC_{50}	0.26 μM	Growth inhibitory potency against NTR-Transfected (nitroreductase) chinese hamster fibroblast known as V79-NTRpuro cell line
V79	IC_{50}	0.26 μM	Antiproliferative activity against chinese hamster V79 NTRpuro cells after 18 hrs
V79	IC_{50}	0.31 μM	Inhibitory activity against V79 (chinese hamster fibroblast) cell line with Escherichia coli nitroreductase combination after 1 hour drug exposure
V79	IC_{50}	0.31 μM	Antiproliferative activity against NTR expressing chinese hamster V79 cells after 1 hr
V79	IC_{50}	183 μM	Therapeutic index, ratio of IC50 for chinese hamster V79 cells to IC50 for Trypanosoma brucei BSF
V79	IC_{50}	254 μM	Inhibitory activity against V79 (chinese hamster fibroblast) cell line without Escherichia coli nitroreductase combination after 72 hours drug exposure
V79	IC_{50}	254 μM	Antiproliferative activity against chinese hamster V79 cells after 72 hrs
V79	IC_{50}	374 μM	Inhibitory activity against V79 (Chinese hamster fibroblast) cell line in chinese hamster
V79	IC_{50}	374 μM	Antiproliferative activity against chinese hamster wild-type V79 NTR-ve cells after 18 hrs
V79	IC_{50}	374000 nM	Cytotoxicity in non-NTR-expressing Chinese hamster fibroblast (V79).
V79	IC_{50}	543 μM	Cytotoxicity against chinese hamster V79 cells after 6 days by Alamar blue assay
V79	IC_{50}	953 μM	Therapeutic index, ratio of IC50 for chinese hamster V79 cells to IC50 for Trypanosoma cruzi
V79	IC_{50}	> 100 μM	Inhibitory activity against V79 (chinese hamster fibroblast) cell line without Escherichia coli nitroreductase combination after 1 hour drug exposure
V79	IC_{50}	> 100 μM	Antiproliferative activity against chinese hamster V79 cells after 1 hr
Vero	IC_{50}	0.57 μM	Antitrypanosomal activity against Trypanosoma cruzi clone Cl-Brener infected in african green monkey Vero cells assessed as growth inhibition after 3 days by luciferase reporter gene assay
Vero	IC_{50}	> 250 μM	Cytotoxicity against african green monkey Vero cells after 6 days by Alamar blue assay
WiDr	IC_{50}	1.14 μM	Antiproliferative activity against human WiDr NTRneo cells after 18 hrs

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	WiDr	IC_{50}	54 μM	Inhibitory activity against WiDr (human colon carcinoma) cell line in human
	WiDr	IC_{50}	54.5 μM	Antiproliferative activity against human wild type WiDr NTR-ve cells after 18 hrs
	WiDr	IC_{50}	54000 nM	Cytotoxicity in non-NTR-expressing human colon carcinoma cell line (WiDr).
	WiDr	IC_{50}	565.4 μM	In vitro cytotoxicity against man colon carcinoma line WiDr cell lines transfected with Escherichia coli B nitroreductase (NTR)
	WiDr-NTR	IC_{50}	1.14 μM	Growth inhibitory potency against NTR-Transfected (nitroreductase) human colon cell line known as WiDr-NTRneo cell line

In Vitro

Tretazicar (CB 1954) (0.1-1000 μM；3 天) 对逆转录病毒转导的 AB22 (AB22-nr) 细胞具有敏感性，IC50 为 3 μM[3]。

受影响细胞中的 DNA 交联形成是由于 Walker 细胞中的酶 DT 脱氢酶 (NAD(P)H 脱氢酶 (醌)) 对该药物进行生物活化，从而还原 Tretazicar 的 4-硝基。该反应的产物是双功能烷化剂 5-氮杂环丙烷-1-基-4-羟氨基-2-硝基苯甲酰胺[4]。

In Vivo

Tretazicar (CB 1954) (80 mg/kg；腹腔注射，第 2 天和第 9 天) 可显著提高存活率[3]。

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.

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 ：125 mg/mL (495.68 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO)

Preparing Stock Solutions	Solvent / Mass / 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

动物实验：

请根据您的 实验动物和给药方式选择适当的溶解方案。

以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用；

以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

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	方案 一 请依序添加每种溶剂： 10% DMSO → 40% PEG300 → 5% Tween-80 → 45% Saline Solubility: ≥ 2.08 mg/mL (8.25 mM); 澄清溶液 此方案可获得 ≥ 2.08 mg/mL（饱和度未知）的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；再向上述体系中加入 50 μL Tween-80，混合均匀；然后再继续加入 450 μL 生理盐水 定容至 1 mL。 生理盐水的配制：将 0.9 g 氯化钠，溶解于 ddH₂O 并定容至 100 mL，可以得到澄清透明的生理盐水溶液。 方案 二 请依序添加每种溶剂： 10% DMSO → 90% (20% SBE-β-CD in Saline) Solubility: ≥ 2.08 mg/mL (8.25 mM); 澄清溶液 此方案可获得 ≥ 2.08 mg/mL（饱和度未知）的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液 中，混合均匀。 2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。
参考文献	[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.

完整储备液配制表：

请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80° C, 6 months; -20° C, 1 month。-80° C 储存时，请在 6 个月内使用，-20° C 储存时，请在 1 个月内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	3.9654 mL	19.8271 mL	39.6542 mL	99.1355 mL
	5 mM	0.7931 mL	3.9654 mL	7.9308 mL	19.8271 mL
	10 mM	0.3965 mL	1.9827 mL	3.9654 mL	9.9136 mL
	15 mM	0.2644 mL	1.3218 mL	2.6436 mL	6.6090 mL
	20 mM	0.1983 mL	0.9914 mL	1.9827 mL	4.9568 mL
	25 mM	0.1586 mL	0.7931 mL	1.5862 mL	3.9654 mL

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	30 mM	0.1322 mL	0.6609 mL	1.3218 mL	3.3045 mL
	40 mM	0.0991 mL	0.4957 mL	0.9914 mL	2.4784 mL
	50 mM	0.0793 mL	0.3965 mL	0.7931 mL	1.9827 mL
	60 mM	0.0661 mL	0.3305 mL	0.6609 mL	1.6523 mL
	80 mM	0.0496 mL	0.2478 mL	0.4957 mL	1.2392 mL
	100 mM	0.0397 mL	0.1983 mL	0.3965 mL	0.9914 mL