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产品名称：曲奥舒凡
产品别名：Treosulfan；NSC 39069; Treosulphan

生物活性：

Description	Treosulfan (NSC 39069;Treosulphan) is an alkylating agent with activity in ovarian cancer and other solid tumor types.
IC_{50} & Target	DNA Alkylator[1]
In Vitro	Treosulfan is an alkylating agent. Treosulfan inhibits several cancer cell lines, such as Panc-1, Miapaca-2 and Capan-2 cells, with IC_{50}s of 3.6 μg/mL, 1.8 μg/mL and 2.1 μg/mL respectively, and shows nearly 100% cytotoxicity on these cell lines at 100 μg/mL. Treosulfan (0.1-100 μg/mL) in combination with gemcitabine exhibits enhanced activity against cancer cells. However, Treosulfan (1, 2.5, 5 μg/ml) combined with 5-fluorouracil (5-FU; 0.1, 0.25, 0.5 μg/ml) has antagonistic effect on Panc-1 cells at intermediate and high concentrations, and on Miapaca-2 cells at all doses[1]. Treosulfan (800 μg/mL) dramatically reduces erythrocyte forward scatter, increases the percentage of annexin-V-binding cells, $[Ca^{2+}]_i$, and ROS. Removal of extracellular Ca^{2+} abrogates the effect of Treosulfan on annexin-V-binding[2].
In Vivo	Treosulfan (1.5 g/kg/day) induces a rapid myeloablation, depletes the splenic B and T cells in mice. Treosulfan (1.5 g/kg/day) causes olny interleukin-2 production in spleen cells for a short time and without obvious significant effect on synthesis of tumor necrosis factor-α and/or interferon-γ in mice[3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (359.32 mM)

H_2O : 50 mg/mL (179.66 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.5932 mL	17.9662 mL	35.9324 mL
	5 mM	0.7186 mL	3.5932 mL	7.1865 mL
	10 mM	0.3593 mL	1.7966 mL	3.5932 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。

In Vivo:

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

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (8.98 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (8.98 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；

	向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (8.98 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.98 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (8.98 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.98 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Nitsch E, et al. Synergistic cytotoxic activity of treosulfan and gemcitabine in pancreatic cancer cell lines. Anticancer Res. 2014 Apr;34(4):1779-84. [2]. Peter T, et al. Programmed erythrocyte death following in vitro Treosulfan treatment. Cell Physiol Biochem. 2015;35(4):1372-80. [3]. Sjöö F, et al. Myeloablative and immunosuppressive properties of treosulfan in mice. Exp Hematol. 2006 Jan;34(1):115-21.

实验参考：

Cell Assay	For cytotoxicity assays, the cells are plated at 1×10^4 cells/mL grown in 100 μL volume per well of 96-well tissue culture plates. The cells are left to adhere overnight and thereafter incubated with different concentrations of Treosulfan alone or in combination with gemcitabine. The drug combination is added to the cell cultures simultaneously or sequentially (the second drug added 12 h after the first). After 72 h of incubation, Alamar Blue® solution is added to the wells prior to further overnight incubation. Absorbance is then measured on a spectrophotometer and cell proliferation and cytotoxicity of drugs are calculated. In some experiments, proliferation and cytotoxicity are also determined by using trypan blue exclusion and cell counting with an improved Neubauer hemocytometer and cell viability assessed by staining the cells with 7-amino-actinomycin D (final concentration 200 μg/mL) and Annexin-V and analyzing via flow cytometry using a FACS Scan flow cytometer[1].
Animal Administration	Mice[3] Female BALB/c mice are 10 to 12 weeks old and weighed approximately 20 g. Animals are fed with standard pelleted food and water ad libitum. They are housed in a climatized chamber with a dark/light cycle of 12 hours. They are divided into four groups: one group is given Treosulfan (1.5 g/kg/day) for 3 consecutive days, one group receives cyclophosphamide (0.1 g/kg/day) for 2 consecutive days, one group is treated with liposomal busulfan (37 mg/kg/day) for 4 consecutive days, and there is a control group with no treatment. Cyclophosphamide, busulfan, and Treosulfan doses are given at sublethal doses to maintain survival of the animals without bone marrow support. Animals are sacrificed on days 1, 3, 6, 9, and 12, after the last dose of treatment, and the spleen and

	femurs are removed. Six animals are included in each time point for the treated animals and two control animals[3].
References	[1]. Nitsch E, et al. Synergistic cytotoxic activity of treosulfan and gemcitabine in pancreatic cancer cell lines. Anticancer Res. 2014 Apr;34(4):1779-84. [2]. Peter T, et al. Programmed erythrocyte death following in vitro Treosulfan treatment. Cell Physiol Biochem. 2015;35(4):1372-80. [3]. Sjöö F, et al. Myeloablative and immunosuppressive properties of treosulfan in mice. Exp Hematol. 2006 Jan;34(1):115-21.