上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：[(3-氨基吡啶-2-基)亚甲基氨基]硫脲
产品别名：3-AP； PAN-811; NSC# 663249; OCX191

生物活性：

Description	3-AP (PAN-811) is a novel inhibitor of the M2 subunit of ribonucleotide reductase (RR), and is a potent radiosensitizer.
IC_{50} & Target	Ribonucleotide reductase (RR)[1]
In Vitro	3-AP (Triapine) is a potent derivative of α-heterocyclic carboxaldehyde thiosemicarbazone (HCT) that inhibits hRRM2 and p53R2 isoforms of the M2 subunit[1]. 3-AP (Triapine) is thought to inhibit ribonucleotide reductase through its preformed iron chelate, rather than directly by removing iron from the active site. In cells containing less topoisomerase IIα fewer DNA strand breaks will be produced, and thus topoisomerase II poisons will be less inhibitory in the K/VP.5 cell line. The IC_{50}s for Dp44mT growth inhibition are 48±9 nM and 60±12 nM, for K562 and K/VP.5 cells, respectively. The IC_{50}s for 3-AP growth inhibition are 476±39 nM and 661±69 nM for K562 and K/VP.5 cells, respectively[2]. PKIH and DpT Fe chelators show high antiproliferative activity against a range of tumor cell lines. Dp44mT shows the greatest antitumor efficacy with an IC_{50} that ranged from 0.005 to 0.4 μM. The average IC_{50} of Dp44mT over 28 cell types is 0.03±0.01 μM, which is significantly lower than that of 3-AP (Triapine; average IC_{50}: 1.41±0.37 μM)[3].
In Vivo	3-AP (Triapine) causes a significant increase (1.7-fold) in splenic weight when expressed as a percentage of total body weight (1.02±0.06%; n=25) compared with control mice (0.6±0.03%; n=27). In the long-term group, a significant increase in heart weight is observed after Dp44mT (0.4 mg/kg per day) (0.8±0.06%; n=4) compared with control mice (0.5±0.01%; n=6). A significant decrease in the expression of Ndrg1, TfR1, and VEGF1 in the liver is noted for Dp44mT- and 3-AP (12 mg/kg per day)-treated animals. The decreased expression could be related to the increased liver Fe in both Dp44mT- and 3-AP-treated mice[3].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 47 mg/mL (240.73 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	5.1219 mL	25.6095 mL	51.2190 mL
5 mM	1.0244 mL	5.1219 mL	10.2438 mL
10 mM	0.5122 mL	2.5610 mL	5.1219 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 (12.80 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (12.80 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 (12.80 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (12.80 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。
References	[1]. Martin LK, et al. A dose escalation and pharmacodynamic study of Triapine and radiation in patients with locally advanced pancreas cancer. Int J Radiat Oncol Biol Phys. 2012 Nov 15;84(4):e475-81. [2]. Yalowich JC, et al. The anticancer thiosemicarbazones Dp44mT and Triapine lack inhibitory effects as catalytic inhibitors or poisons of DNA topoisomerase IIα. Biochem Pharmacol. 2012 Jul 1;84(1):52-8. [3]. Whitnall M, et al. A class of iron chelators with a wide spectrum of potent antitumor activity that overcomes resistance to chemotherapeutics. Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14901-6.

实验参考：

Cell Assay	An MTT assay is used to determine cell growth inhibition of CHO cells. Human leukemia K562 cells and K/VP.5 cells (a 26-fold etoposide-resistant K562-derived sub-line with decreased levels of topoisomerase IIα mRNA and protein) are maintained as suspension cultures in MEM containing 10% fetal calf serum (FCS). For growth inhibition assays, K562 and K/VP.5 cells are plated at a concentration of 1.5×10^5 cell/mL, and incubated 5 d with various concentrations of Dp44mT, 3-AP or vehicle (DMSO) for 48 h, after which cells are counted on a model ZBF Coulter counter. The IC_{50} growth inhibitory concentration for each cell line is calculated from a non-linear least-squares fit to a 2-parameter logistic equation[2].
Animal Administration	Mice[3] Female BALB/c nu/nu mice are used at 8-10 weeks of age. Tumor cells in culture are harvested, and 10^7 cells are suspended in Matrigel and injected s.c. into the right flanks of mice. After engraftment, tumor size is measured by Vernier calipers. Tumor volumes (in cubic millimeters) are calculated. When tumor volumes reached 120 mm^3, i.v. treatment began (day 0). Chelators (e.g., 3-AP) are dissolved in 15% propylene glycol in 0.9% saline and injected i.v. over 5 consecutive days per week for up to 7 weeks. Control mice are treated with vehicle alone.
References	[1]. Martin LK, et al. A dose escalation and pharmacodynamic study of Triapine and radiation in patients with locally advanced pancreas cancer. Int J Radiat Oncol Biol Phys. 2012 Nov 15;84(4):e475-81. [2]. Yalowich JC, et al. The anticancer thiosemicarbazones Dp44mT and Triapine lack inhibitory effects as catalytic inhibitors or poisons of DNA topoisomerase IIα. Biochem Pharmacol. 2012 Jul 1;84(1):52-8.

	[3]. Whitnall M, et al. A class of iron chelators with a wide spectrum of potent antitumor activity that overcomes resistance to chemotherapeutics. Proc Natl Acad Sci U S A. 2006 Oct 3;103(40):14901-6.