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产品名称：安吖啶
产品别名：Amsacrine；m-AMSA; acridinyl anisidide

生物活性：

Description	Amsacrine (m-AMSA; acridinyl anisidide) is an inhibitor of topoisomerase II, and acts as an antineoplastic agent which can intercalates into the DNA of tumor cells.
IC_{50} & Target	Topoisomerase II
In Vitro	Amsacrine (m-AMSA) blocks HERG currents in HEK 293 cells and Xenopus oocytes in a concentration-dependent manner, with IC_{50} values of 209.4 nm and 2.0 μM, respectively. Amsacrine (m-AMSA) causes a negative shift in the voltage dependence of both activation (−7.6 mV) and inactivation (−7.6 mV). HERG current block by amsacrine is not frequency dependent[1]. In vitro studies of normal human lymphocytes with various concentrations of Amsacrine (m-AMSA), show both increased levels of chromosomal aberrations, ranging from 8% to 100%, and increase SCEs, ranging from 1.5 times the normal at the lowest concentration studied (0.005 μg/mL) to 12 times the normal (0.25 μg/mL)[3]. Amsacrine (m-AMSA)-induced apoptosis of U937 cells is characterized by caspase-9 and caspase-3 activation, increased intracellular Ca^{2+} concentration, mitochondrial depolarization, and MCL1 down-regulation. Amsacrine (m-AMSA) induces MCL1 down-regulation by decreasing its stability. Further, amsacrine-treated U937 cells show AKT degradation and Ca^{2+}-mediated ERK inactivation[4].
In Vivo	In animals treated with different doses of amsacrine (0.5-12 mg/kg), the frequencies of micronucleated polychromatic erythrocytes increase significantly after treatment with 9 and 12 mg/kg. Furthermore, the present study demonstrates for the first time that Amsacrine (m-AMSA) has high incidences of clastogenicity and low incidences of aneugenicity whereas nocodazole has high incidences of aneugenicity and low incidences of clastogenicity during mitotic phases in vivo[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 9.3 mg/mL (23.64 mM;** Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5416 mL	12.7078 mL	25.4155 mL
5 mM	0.5083 mL	2.5416 mL	5.0831 mL
10 mM	0.2542 mL	1.2708 mL	2.5416 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 (6.35 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.35 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。
References	[1]. Thomas D, et al. Inhibition of cardiac HERG currents by the DNA topoisomerase II inhibitor amsacrine: mode of action. Br J Pharmacol. 2004 Jun;142(3):485-94. [2]. Attia SM. Molecular cytogenetic evaluation of the mechanism of genotoxic potential of amsacrine and nocodazole in mouse bone marrow cells. J Appl Toxicol. 2013 Jun;33(6):426-33. [3]. Kao-Shan CS, et al. Cytogenetic effects of amsacrine on human lymphocytes in vivo and in vitro. Cancer Treat Rep. 1984 Jul-Aug;68(7-8):989-97. [4]. Lee YC, et al. Amsacrine-induced apoptosis of human leukemia U937 cells is mediated by the inhibition of AKT- and ERK-induced stabilization of MCL1. Apoptosis. 2016 Oct 19

实验参考：

Animal Administration	Amsacrine (m-AMSA) is investigated in three separated experiments. In the first experiment, animals are treated by intraperitoneal injection with 0.5, 1.5 and 4.5 mg/kg of amsacrine and bone marrow is sampled 24 h after treatment. Preliminary negative MN results at this sampling time lead to the use of 30 h sampling time for amsacrine. Thus, in the second experiment, mice are treated with 0.5, 1.5 and 4.5 mg/kg of Amsacrine (m-AMSA) and bone marrow is sampled 30 h after treatment. The doses and sampling times for amsacrine are chosen by reference to earlier studies and the selected doses are within the dose range used for human chemotherapy. The results again show that the micronuclei frequency in the bone marrow of mice is not affected by treatment with any of the selected doses of the test agent, at 30 h sampling time, thus, in the third experiment, mice are treated with 6, 9 and 12 mg/kg of amsacrine and bone marrow is sampled 24 and 30 h after treatment. [2]
References	[1]. Thomas D, et al. Inhibition of cardiac HERG currents by the DNA topoisomerase II inhibitor amsacrine: mode of action. Br J Pharmacol. 2004 Jun;142(3):485-94. [2]. Attia SM. Molecular cytogenetic evaluation of the mechanism of genotoxic potential of amsacrine and nocodazole in mouse bone marrow cells. J Appl Toxicol. 2013 Jun;33(6):426-33. [3]. Kao-Shan CS, et al. Cytogenetic effects of amsacrine on human lymphocytes in vivo and in vitro. Cancer Treat Rep. 1984 Jul-Aug;68(7-8):989-97. [4]. Lee YC, et al. Amsacrine-induced apoptosis of human leukemia U937 cells is mediated by the inhibition of AKT- and ERK-induced stabilization of MCL1. Apoptosis. 2016 Oct 19