上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
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产品名称：Astemizole
CAS 号：68844-77-9
产品货号：S87909

生物活性：

Description	Astemizole (R 43512) 是一个长效的二代抗组胺活性分子，是常用的抗过敏活性分子，是组胺 H1 受体 (histamine H1-receptor) 的拮抗剂，IC50 值为 4 nM。Astemizole 同时还具有 hERG K+ 通道的阻断活性，IC50 值为 0.9 nM。Astemizole 还具有抗胆碱能和止痒作用。
IC50 & Target	H1 Receptor

Cellular Effect

Cell Line	Type	Value	Description
CHO	IC_{50}	1.1 μM	Inhibition of Cav1.2 current measured using QPatch automatic path clamp system in CHO cells expressing Cav1.2, beta-2 and alpha-2/delta-1 subunits
CHO	IC_{50}	29.6 μM	Cytotoxicity against CHO cells measured after 48 hrs by MTT assay
CHO	IC_{50}	29.6 μM	Cytotoxicity against CHO cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay
HEK293	IC_{50}	0.008 μM	Inhibition of human ERG expressed in HEK293 cells coexpressing Kir2.3 after 30 mins by FluxOR based FLIPR assay
HEK293	IC_{50}	0.023 μM	Displacement of [3H] dofetilide from human ERG channel expressed in HEK293 cell membranes incubated for 2 hrs by scintillation counting analysis
HEK293	IC_{50}	0.9 nM	Inhibition of hERG potassium channel in HEK293 cells by patch clamp assay
HEK293	IC_{50}	14 nM	Inhibition of [3H]-astemizole binding to human ERG expressed in HEK293 cell membranes by scintillation counting method
HEK293	IC_{50}	2.6 nM	Displacement of [3H]Astemizole from human recombinant ERG expressed in HEK293 cells at after 60 mins
HEK293	IC_{50}	2.6 μM	Inhibition of human ERG expressed in HEK293 cells measured after 30 mins by FluxOR dye based FLIPR TETRA assay
HEK293	IC_{50}	26.4 μM	Inhibition of human MATE1-mediated ASP+ uptake expressed in HEK293 cells after 1.5 mins by fluorescence assay
HEK293	IC_{50}	5.1 μM	Cytotoxicity against human ERG transfected HEK293 cells after 24 hrs by MTT assay
HepG2	IC_{50}	7.97 μM	Cytotoxicity against human HepG2 cells after 24 hrs by MTT assay
HT-29	IC_{50}	15.4 μM	Cytotoxicity against human HT-29 cells after 24 hrs by MTT assay
LLC-PK1	IC_{50}	1.3 μM	Inhibition of P-glycoprotein, human L-MDR1 expressed

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				in LLC-PK1 epithelial cells using calcein-AM polarisation assay
	LLC-PK1	IC_{50}	1.3 μM	Inhibition of P-glycoprotein, mouse L-mdr1a expressed in LLC-PK1 epithelial cells using calcein-AM polarisation assay
	LLC-PK1	IC_{50}	1.7 μM	Inhibition of P-glycoprotein, mouse L-mdr1b expressed in LLC-PK1 epithelial cells using calcein-AM polarisation assay
	RBL-2H3	IC_{50}	0.0533 μM	Antiallergic activity in rat RBL2H3 cells assessed as inhibition of C48/80-induced mast cell degranulation preincubated with compound for 30 mins and then treated with C48/80 for 1 hr by neutral red dye based method
	RBL-2H3	IC_{50}	0.0819 μM	Antiallergic activity in rat RBL2H3 cells assessed as inhibition of C48/80-induced histamine release preincubated with compound for 30 mins followed by C48/80 stimulation for 1 hr
	RBL-2H3	IC_{50}	0.156 μM	Antiallergic activity in IgE/Ag-stimulated rat RBL2H3 cells assessed as inhibition of HSA-induced beta-hexosaminidase release preincubated with compound for 30 mins and then stimulated with HSA for 15 mins followed by incubation with P-nitrophenyl-N-acety
	Vero C1008	EC_{50}	1.1 μM	Determination of antiviral efficacy in high-content imaging assay in Vero E6 cells infected with SARS-CoV-2 (USA-WA1/2020 isolate) at MOI 0.75 after 24 hrs

In Vivo

Astemizole (po，10 和 30 mg/kg) 和 (iv，1 和 3 mg/kg) 对呼吸率、心率和血压无影响，即使在 30 mg/kg 和 3 mg/kg 的高剂量下，对雄性普通狨猴的体温和运动能力也无影响。 但 Astemizole 在 30 mg/kg (po) 和 1 mg/kg (iv) 时可延长 QT 间期并诱发室性早搏[3]。

Astemizole (po、3 和 30 mg/kg) 在剂量为 3 mg/kg 时，室性率、QT 间期和 QTcF 的给药前控制值 (C) 分别为 31 次/分钟、319 ms 和 256，而这些分别为 31 次/分钟、331 ms 和 270 在小鼠中分别以 30 mg/kg 的剂量给药。 此外，剂量为 30 mg/kg (po) 的 Astemizole 可能通过抑制 hERG K+ 通道引起尖端扭曲性室性心动过速[4]。

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 ：125 mg/mL (272.59 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	2.1807 mL	10.9035 mL	21.8069 mL
	5 mM	0.4361 mL	2.1807 mL	4.3614 mL
	10 mM	0.2181 mL	1.0903 mL	2.1807 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

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	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 方案 一 请依序添加每种溶剂： 10% DMSO → 40% PEG300 → 5% Tween-80 → 45% Saline Solubility: ≥ 6.25 mg/mL (13.63 mM); 澄清溶液 此方案可获得 ≥ 6.25 mg/mL（饱和度未知）的澄清溶液。 以 1 mL 工作液为例，取 100 μL 62.5 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% Corn Oil Solubility: ≥ 6.25 mg/mL (13.63 mM); 澄清溶液 此方案可获得 ≥ 6.25 mg/mL（饱和度未知）的澄清溶液，此方案实验周期在半个月以上的动物实验酌情使用。 以 1 mL 工作液为例，取 100 μL 62.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
参考文献	[1]. Laduron PM, et al. In vitro and in vivo binding characteristics of a new long-acting histamine H1 antagonist, astemizole. Mol Pharmacol. 1982 Mar;21(2):294-300. [2]. Richards DM, et al. Astemizole. A review of its pharmacodynamic properties and therapeutic efficacy. Drugs. 1984 Jul;28(1):38-61. [3]. Ikuo Horii, et al. Development of telemetry system in the common marmoset--cardiovascular effects of astemizole and nicardipine. J Toxicol Sci. 2002 May;27(2):123-30. [4]. Hiroko Izumi-Nakaseko, et al. Possibility as an anti-cancer drug of astemizole: Evaluation of arrhythmogenicity by the chronic atrioventricular block canine model. J Pharmacol Sci. 2016 Jun;131(2):150-3.

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

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DMSO	**1 mM**	2.1807 mL	10.9035 mL	21.8069 mL	54.5173 mL
	5 mM	0.4361 mL	2.1807 mL	4.3614 mL	10.9035 mL
	10 mM	0.2181 mL	1.0903 mL	2.1807 mL	5.4517 mL
	15 mM	0.1454 mL	0.7269 mL	1.4538 mL	3.6345 mL
	20 mM	0.1090 mL	0.5452 mL	1.0903 mL	2.7259 mL
	25 mM	0.0872 mL	0.4361 mL	0.8723 mL	2.1807 mL
	30 mM	0.0727 mL	0.3634 mL	0.7269 mL	1.8172 mL
	40 mM	0.0545 mL	0.2726 mL	0.5452 mL	1.3629 mL
	50 mM	0.0436 mL	0.2181 mL	0.4361 mL	1.0903 mL
	60 mM	0.0363 mL	0.1817 mL	0.3634 mL	0.9086 mL
	80 mM	0.0273 mL	0.1363 mL	0.2726 mL	0.6815 mL
	100 mM	0.0218 mL	0.1090 mL	0.2181 mL	0.5452 mL