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产品名称: 马来到匹杉琼

产品别名: **Pixantrone dimaleate; BBR 2778 dimaleate; 马来酸匹杉琼**

生物活性:					
Description		Pixantrone dimaleate is a topoisomerase II inhibitor and DNA intercalator, with anti-tumor activity.			
IC ₅₀ & Target		Topoisomerase II			
In Vitro		<p>Pixantrone dimaleate is a topoisomerase II inhibitor. Pixantrone induces cell death in multiple cancer cell lines independent of cell cycle perturbation, with IC₅₀s of 37.3 nM, 126 nM and 136 nM for T47D, MCF-10A and OVCAR5 cells, respectively. Pixantrone induces DNA damage at high concentrations (500 nM) but not at concentrations (100 nM) sufficient to kill PANC1 cells. Pixantrone (25 or 100 nM) induces severe chromosomal aberrations and mitotic catastrophe in PANC1 cells. Pixantrone (100 nM) may disrupt chromosome segregation because of generating merotelic kinetochore attachments that cause chromosome non-disjunction^[1]. Pixantrone potently inhibits growth of human Leukemia K562 cells, etoposide-resistant K/VP.5 cells, MDCK and ABCB1-transfected MDCK/MDR cells, with IC₅₀s of 0.10 μM, 0.56 μM, 0.058 μM and 4.5 μM, respectively. Pixantrone (0.01-0.2 μM) leads to a concentration-dependent formation of linear DNA through acting on topoisomerase IIα. Pixantrone produces semiquinone free radicals in an enzymatic reducing system, although not in a cellular system, most likely due to low cellular uptake^[2]. Pixantrone (0.01-10 μM) shows potent inhibitory activities against rat 97-116 peptide-specific T cell proliferation^[4].</p>			
In Vivo		<p>Pixantrone (27 mg/kg) does not worsen pre-existing moderate degenerative cardiomyopathy in doxorubicin-pretreated mice, by i.v. one dose every 7 days repeated thrice (q7d × 3). Pixantrone (27 mg/kg) causes minimal cardiotoxic in mice following repeated treatment cycles. Moreover, Pixantrone results in less mortality than mitoxantrone in doxorubicin-pretreated mice^[3]. Pixantrone (16.25 mg/kg i.v, q7d × 3) modulates Lymph node cells (LNC) responses, and affects T cell subpopulations in TACHR-immunized Lewis rats. Pixantrone also shows preventive and therapeutic effect in experimental autoimmune myasthenia gravis (EAMG) rats^[4].</p>			
<p>In Vitro: DMSO : 33.33 mg/mL (59.78 mM; Need ultrasonic) H₂O : 16.67 mg/mL (29.90 mM; Need ultrasonic)</p>					
Preparing Stock Solutions		<div>Solvent / Mass / Concentration</div>	1 mg	5 mg	10 mg
		1 mM	1.7937 mL	8.9684 mL	17.9369 mL
		5 mM	0.3587 mL	1.7937 mL	3.5874 mL
		10 mM	0.1794 mL	0.8968 mL	1.7937 mL
<p>*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。</p> <p>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。</p> <p>In Vivo:</p> <p>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:</p>					



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Solvent&Solubility	<p>——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</p> <p>1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 2.5 mg/mL (4.48 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (4.48 mM, 饱和度未知) 的澄清溶液。</p> <p>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。</p> <p>2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2.5 mg/mL (4.48 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (4.48 mM, 饱和度未知) 的澄清溶液。</p> <p>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。</p>
References	<p>[1]. Beeharry N, et al. Pixantrone induces cell death through mitotic perturbations and subsequent aberrant cell divisions. <i>Cancer Biol Ther.</i> 2015;16(9):1397-406.</p> <p>[2]. Hasinoff BB, et al. Mechanisms of Action and Reduced Cardiotoxicity of Pixantrone; a Topoisomerase II Targeting Agent with Cellular Selectivity for the Topoisomerase IIα Isoform. <i>J Pharmacol Exp Ther.</i> 2016 Feb;356(2):397-409.</p> <p>[3]. Cavalletti E, et al. Pixantrone (BBR 2778) has reduced cardiotoxic potential in mice pretreated with doxorubicin: comparative studies against doxorubicin and mitoxantrone. <i>Invest New Drugs.</i> 2007 Jun;25(3):187-95.</p> <p>[4]. Ubiali F, et al. Pixantrone (BBR2778) reduces the severity of experimental autoimmune myasthenia gravis in Lewis rats. <i>J Immunol.</i> 2008 Feb 15;180(4):2696-703.</p>
实验参考:	
Cell Assay	<p>Briefly, cells seeded into 96-well plates are treated with increasing concentrations of either pixantrone or doxorubicin for 72 hours. After this time, MTS reagent is added to cells and incubated at 37°C for a further 4 hours. Cell proliferation is then determined by measuring the absorbance at 490 nm. All data points are normalized to untreated cells. All treatments are performed in triplicate and performed a minimum of 3 times^[1].</p>
	<p>Mice[3]</p> <p>To evaluate the potential cardiotoxicity of Pixantrone in doxorubicin-pretreated mice, doxorubicin 7.5 mg/kg is administered intravenously every 7 days for 3 weeks (1 cycle) to a group of CD1 females. Six weeks later, these mice receive either 0.9% saline (vehicle), doxorubicin 7.5 mg/kg, Pixantrone 27 mg/kg, or mitoxantrone 3 mg/kg intravenously every 7 days for 3 weeks (2 cycles). Animals are sacrificed after the first cycle at 8 weeks, and after the second cycle at 16 weeks. In addition, to evaluate the potential cardiotoxicity of Pixantrone as a single agent compared with doxorubicin and mitoxantrone, CD1 female mice receive a single or a double cycle of vehicle, doxorubicin 7.5 mg/kg, Pixantrone 27 mg/kg, or mitoxantrone 3 mg/kg. These animals are sacrificed after the first and second cycles (at 8 and 16 weeks, all groups), during week 14 (Pixantrone-treated group only) and</p>



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Animal Administration	<p>during week 22 (Pixantrone- and vehicle-treated groups)[3].</p> <p>Rats[4]</p> <p>For the studies on Pixantrone efficacy on EAMG, TACHR-immunized rats are randomly assigned to different treatment groups: 1) preventive Pixantrone group, starting 4 days after immunization, with 16.25 mg/kg Pixantrone, administered i.v. via tail vein, once a week for three times; 2) therapeutic Pixantrone group, starting 4 wk after immunization, with 16.25 mg/kg Pixantrone, administered i.v. via tail vein, once a week for three times; 3) therapeutic MTX group (1.2 mg/kg, i.v. via tail vein, once a week for three times); and 4) vehicle group (sterile saline, i.v. via tail vein, once a week for three times). The doses of Pixantrone and MTX used in this study are in both cases equal to one-fourth of the LD10 for single i.v. injection in rats. Treatment assignment is performed at day 4 after TACHR immunization (preventive schedule) in coincidence of the acute phase of EAMG, or at onset of clinical signs (therapeutic schedule), which occurs after 4 wk. Animals are sacrificed after deep anesthesia obtained by carbon dioxide; low-grade anesthesia with chloral hydrate administered i.p. is used for TACHR immunization and drug treatments[4].</p>
References	<p>[1]. Beeharry N, et al. Pixantrone induces cell death through mitotic perturbations and subsequent aberrant cell divisions. <i>Cancer Biol Ther.</i> 2015;16(9):1397-406.</p> <p>[2]. Hasinoff BB, et al. Mechanisms of Action and Reduced Cardiotoxicity of Pixantrone; a Topoisomerase II Targeting Agent with Cellular Selectivity for the Topoisomerase IIα Isoform. <i>J Pharmacol Exp Ther.</i> 2016 Feb;356(2):397-409.</p> <p>[3]. Cavalletti E, et al. Pixantrone (BBR 2778) has reduced cardiotoxic potential in mice pretreated with doxorubicin: comparative studies against doxorubicin and mitoxantrone. <i>Invest New Drugs.</i> 2007 Jun;25(3):187-95.</p> <p>[4]. Ubiali F, et al. Pixantrone (BBR2778) reduces the severity of experimental autoimmune myasthenia gravis in Lewis rats. <i>J Immunol.</i> 2008 Feb 15;180(4):2696-703.</p>

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