产品名称：盐酸去甲维拉帕米
产品别名：Norverapamil hydrochloride

生物活性：

Description	Norverapamil hydrochloride ((±)-Norverapamil hydrochloride), an N-demethylated metabolite of Verapamil, is a L-type calcium channel blocker and a P-glycoprotein (P-gp) function inhibitor[1][2].
IC_{50} & Target	Calcium channel blocker[1] P-glycoprotein (P-gp) inhibitor[2]
In Vitro	Norverapamil hydrochloride ((±)-Norverapamil hydrochloride) is similarly effective as verapamil at inhibiting isoniazid and rifampicin tolerance and killing of intracellular M. tuberculosis in the absence of other drugs. norverapamil, also inhibits macrophage-induced tolerance and achieves similar serum levels to verapamil[1]. Verapamil and its major metabolite norverapamil were identified to be both mechanism-based inhibitors and substrates of CYP3A and reported to have non-linear pharmacokinetics in clinic[3].
In Vivo	Norverapamil hydrochloride (9 mg/kg; p.o.), a major metabolite of verapamil, has terminal half-life, AUC and Cmax values of 9.4 hours, 260 ng•h/ml, and 41.6 ng/mL, respectively[4].

Animal Model:	Male Sprague-Dawley rats[3]
Dosage:	9 mg/kg (Pharmacokinetic Study)
Administration:	Oral administration
Result:	$t_{1/2}$=9.4 hours; AUC=260 ng•h/mL; C_{max}=41.6 ng/mL.

Solvent&Solubility

In Vitro:

H_2O : ≥ 50 mg/mL (104.81 mM)

DMSO : ≥ 31 mg/mL (64.98 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0963 mL	10.4813 mL	20.9626 mL
	5 mM	0.4193 mL	2.0963 mL	4.1925 mL
	10 mM	0.2096 mL	1.0481 mL	2.0963 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 (5.24 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.24 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 (5.24 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.24 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]. Adams KN, et al. Verapamil, and its metabolite norverapamil, inhibit macrophage-induced, bacterial efflux pump-mediated tolerance to multiple anti-tubercular drugs. J Infect Dis. 2014 Aug 1;210(3):456-66. [2]. Pauli-Magnus C, et al. Characterization of the major metabolites of verapamil as substrates and inhibitors of P-glycoprotein. J Pharmacol Exp Ther. 2000 May;293(2):376-82. [3]. Wang J et al. A semi-physiologically-based pharmacokinetic model characterizing mechanism-based auto-inhibition to predict stereoselective pharmacokinetics of verapamil and its metabolite norverapamil in human. Eur J Pharm Sci. 2013 Nov 20;50(3-4):290-302. [4]. Choi DH, et al. Effects of simvastatin on the pharmacokinetics of verapamil and its main metabolite, norverapamil, in rats. Eur J Drug Metab Pharmacokinet. 2009 Jul-Sep;34(3-4):163-8.