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产品名称：INNO-206
产品别名：Aldoxorubicin； DOXO-EMCH

生物活性：

Description	Aldoxorubicin (INNO-206) is an albumin-binding prodrug of Doxorubicin (DNA topoisomerase II inhibitor), which is released from albumin under acidic conditions. Aldoxorubicin (INNO-206) has potent antitumor activities in various cancer cell lines and in murine tumor models.
IC_{50} & Target	Topoisomerase II　Daunorubicins/Doxorubicins
In Vitro	Aldoxorubicin (INNO-206) (0.27 to 2.16 μM) inhibits blood vessel formation and reduces multiple myeloma cell growth in a pH-dependent fashion[1].
In Vivo	Aldoxorubicin (INNO-206) (10.8 mg/kg, i.v.) shows significantly smaller tumor volumes and IgG levels on days 28, and is well tolerated with 90% of mice surviving until the termination of the study in the mice bearing the LAGκ-1A tumor[1]. Aldoxorubicin (INNO-206) shows a good safety profile at doses up to 260 mg/mL doxorubicin equivalents, and is able to induce tumor regressions in breast cancer, small cell lung cancer and sarcoma in phase I study[2]. Aldoxorubicin (INNO-206) shows superior activity over doxorubicin in a murine renal cell carcinoma model and in breast carcinoma xenograft models[3].

Solvent&Solubility

In Vitro:

DMSO : 75 mg/mL (99.90 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.3320 mL	6.6600 mL	13.3200 mL
	5 mM	0.2664 mL	1.3320 mL	2.6640 mL
	10 mM	0.1332 mL	0.6660 mL	1.3320 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；该产品在溶液状态不稳定，建议您现用现配，即刻使用。

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 (3.33 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (3.33 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 (3.33 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (3.33 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (3.33 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.33 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 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 玉米油中，混合均匀。
References	[1]. Eric Sanchez, et al. Anti-Myeloma Effects of the Novel Anthracycline Derivative INNO-206. Clin Cancer Res.2012 18; 3856. [2]. Kratz, F. INNO-206 (DOXO-EMCH), an Albumin-Binding Prodrug of Doxorubicin Under Development for Phase II Studies. Current Bioactive Compounds, 2011, 7(1): 33-38(6) [3]. Graeser R, et al. INNO-206, the (6-maleimidocaproyl hydrazone derivative of doxorubicin), shows superior antitumor efficacy compared to doxorubicin in different tumor xenograft models and in an orthotopic pancreas carcinoma model. Invest New Drugs. 2010 F [4]. Walker L, et al. Cell penetrating peptides fused to a thermally targeted biopolymer drug carrier improve the delivery and antitumor efficacy of an acid-sensitive doxorubicin derivative. Int J Pharm. 2012 Oct 15;436(1-2):825-32.

实验参考：

Cell Assay	Cells are seeded at 1×10^5 cells/100 μL/well in 96-well plates in RPMI-1640 media with FBS for 24 hours before treatment. Cells are cultured in the presence of medium, Aldoxorubicin (INNO-206) or doxorubicin for 48 hours. Next, cell viability is quantified using the CellTiter 96 AQueous Non-Radioactive Cell Proliferation Assay. Each well is treated with MTS for 1 to 4 hours, after which absorbance at 490 nm is recorded using a 96-well plate reader. The quantity of formazan product as measured is directly proportional to the number of living cells. Data graphed are means±SEM using 3 replicates per data point.
Animal Administration	For the LAGκ-1A experiment, Aldoxorubicin (INNO-206) is administered to SCID mice at 10.8 mg/kg (doxorubicin equivalent dose of 8.0 mg/kg) once weekly. Mice are treated with conventional doxorubicin at 4.0 and 8.0 mg/kg once weekly. For the LAGκ-2 experiment, Aldoxorubicin (INNO-206) is administered once weekly (W) at doses of 2.7 and 5.4 mg/kg, or on 3 consecutive days (W-F) weekly at doses of 0.9 and 1.8 mg/kg. Bortezomib is administered twice weekly (W, F) at a dose of 0.5 mg/kg. Doxorubicin is administered to SCID mice at 2, 4, and 8 mg/kg, and PLD is administered to SCID mice at 2 mg/kg once weekly. Each drug is administered i.v. in a volume of 100 μL.
References	[1]. Eric Sanchez, et al. Anti-Myeloma Effects of the Novel Anthracycline Derivative INNO-206. Clin Cancer Res.2012 18; 3856. [2]. Kratz, F. INNO-206 (DOXO-EMCH), an Albumin-Binding Prodrug of Doxorubicin Under Development for Phase II Studies. Current Bioactive Compounds, 2011, 7(1): 33-38(6) [3]. Graeser R, et al. INNO-206, the (6-maleimidocaproyl hydrazone derivative of doxorubicin),

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