上海源叶生物科技有限公司
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产品名称：GS-441524
CAS 号：1191237-69-0
产品货号：S87677

生物活性：

Description	GS-441524 是 Remdesivir 的主要活性代谢物，活性更优于 Remdesivir ，感染病毒的原代人肺和猫细胞的细胞模型中显示出相似的活性。 GS-441524 对猫传染性腹膜炎病毒 (FIPV) 有较强的抑制作用，对应的 EC50 值为 0.78 μM。
IC50 & Target	EC50: 0.78 μM (FIPV)[1].

Cellular Effect

Cell Line	Type	Value	Description
Fibroblast	CC_{50}	> 100 μM	Cytotoxicity against mock-infected human embryonic lung fibroblast cells incubated for 5 days by MTS assay
HEL 299	CC_{50}	> 100 μM	Cytotoxicity against HEL 299 cells assessed as reduction in cell viability measured after 1 to 2 hrs by MTS colorimetric assay
HeLa	EC_{50}	> 20 μM	Antiviral activity against Ebolavirus Kikwit infected in human HeLa cells assessed as reduction in viral glycoprotein levels preincubated with cells for 2 hrs followed by viral infection measured after 48 hrs by immunostaining based assay
HeLa	CC_{50}	> 20 μM	Cytotoxicity against human HeLa after 4 to 5 days by Cell-Titer Glo viability assay
HeLa	EC_{50}	> 20 μM	Antiviral activity against Ebolavirus infected in human HeLa cells after 48 hrs by immuno-staining assay
HeLa	CC_{50}	> 30 μM	Cytotoxicity against human HeLa cells by MTS assay
HeLa	EC_{50}	11 μM	Antiviral activity against Yellow fever virus 17D infected in human HeLa cells assessed as inhibition of virus induced cytopathic effect after 24 hrs by MTS assay
HEp-2	CC_{50}	> 100 μM	Cytotoxicity against human Hep2 cells assessed as reduction in cell viability after 4 to 5 days by Cell-Titer Glo assay
HEp-2	CC_{50}	> 100 μM	Cytotoxicity against human HEp-2 cells assessed as reduction in cell viability incubated for 4 to 5 days by CellTiter Glo viability assay
HEp-2	IC_{50}	0.35 μM	Drug metabolism in human HEp-2 cells assessed as 1-NTP metabolite concentration at EC50 over 48 hrs by LC-MS/MS analysis
Huh-7	CC_{50}	> 20 μM	Cytotoxicity against human HuH7 after 4 to 5 days by Cell-Titer Glo viability assay
Huh-7	CC_{50}	> 88 μM	Cytotoxicity against human HuH7 cells assessed as reduction in cell viability after 3 days by calcein-AM dye based fluorescence assay
Huh-7	CC_{50}	> 89 μM	Cytotoxicity against human HuH7 cells by MTS assay

	Huh-7	CC_{50}	> 89 µM	Cytotoxicity against human Huh-7 cells assessed as reduction in cell viability measured after 3 days by dual-Glo luciferase assay
	Huh-7	EC_{50}	4.1 µM	Antiviral activity against Hepatitis C virus genotype 1b infected in human HuH7 cells assessed as inhibition of virus induced cytopathic effect after 24 hrs by MTS assay
	Macrophage	CC_{50}	> 20 µM	Cytotoxicity against human primary macrophages after 4 to 5 days by Cell-Titer Glo viability assay
	MDCK	CC_{50}	> 30 µM	Cytotoxicity against dog MDCK cells by MTS assay
	MDCK	EC_{50}	27.9 µM	Antiviral activity against Influenza A virus H3N2 infected in MDCK cells assessed as inhibition of virus induced cytopathic effect after 24 hrs by MTS assay
	MRC5	EC_{50}	> 30 µM	Antiviral activity against Coxsackievirus A7 infected in human MRC5 cells assessed as inhibition of virus induced cytopathic effect after 24 hrs by MTS assay
	MRC5	EC_{50}	> 30 µM	Antiviral activity against Coxsackievirus A21 infected in human MRC5 cells assessed as inhibition of virus induced cytopathic effect after 24 hrs by MTS assay
	MRC5	CC_{50}	> 30 µM	Cytotoxicity against human MRC5 cells by MTS assay
	MT4	CC_{50}	> 50 µM	Cytotoxicity against human MT4 cells assessed as reduction in cell viability measured after 5 days by CellTiter Glo viability assay
	MT4	CC_{50}	> 57 µM	Cytotoxicity against human MT4 cells assessed as reduction in cell viability after 4 to 5 days by Cell-Titer Glo assay
	Vero	EC_{50}	> 30 µM	Antiviral activity against West nile virus NY99 infected in african green monkey Vero cells assessed as inhibition of virus induced cytopathic effect after 24 hrs by MTS assay
	Vero	CC_{50}	> 30 µM	Cytotoxicity against african green monkey Vero cells by MTS assay
	Vero	CC_{50}	> 30 µM	Cytotoxicity against african green monkey Vero E6 cells by MTS assay
	Vero	EC_{50}	1.71 µM	Antiviral activity against Parainfluenza 3 C 243 infected in african green monkey Vero cells assessed as inhibition of virus induced cytopathic effect after 24 hrs by MTS assay
	Vero	EC_{50}	2.24 µM	Antiviral activity against SARS coronavirus Toronto-2 infected in african green monkey Vero cells assessed as inhibition of virus induced cytopathic effect after 24 hrs by MTS assay
	Vero	EC_{50}	9.46 µM	Antiviral activity against Dengue virus type 2 New

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				Guinea C infected in african green monkey Vero E6 cells assessed as inhibition of virus induced cytopathic effect after 24 hrs by MTS assay
	Vero C1008	CC_{50}	72.38 μM	Cytotoxicity against African green monkey Vero E6 cells assessed as reduction in cell viability incubated for 1 to 2 hrs by MTS assay
	Vero C1008	CC_{50}	72.9 μM	Cytotoxicity against African green monkey Vero E6 cells assessed as reduction in cell viability measured after 1 to 2 hrs by MTS colorimetric assay Cytotoxicity against African green monkey Vero E6 cells assessed as reduction in cell viability measured after 1 to 2 hrs by MTS colorimetric assay

In Vitro

在所有浓度的 GS-441524 (1.2-100 μM; 24 h) 下，细胞均正常出现并生长，并且在 24 小时后无法吸收荧光染料 CellTox Green。因此，细胞毒性浓度 -50% (CC50) >100 μM。GS-441524 的有效浓度 -50% (EC50) 计算为 0.78 μM[1]。

In Vivo

所有 10 只接受治疗的猫对治疗均有快速反应，淋巴细胞水平和直肠温度均恢复到感染前水平和两只无症状猫的水平。所有十只接受过一次或两次治疗的猫迄今为止 (感染后超过八个月) 均保持正常。注射会导致一些猫在化合物给药后 10 秒内出现短暂的“刺痛”反应。局部和短暂的疼痛表现为异常姿势、舔注射部位和/或发声，注射后持续约 30-60 秒。一些动物的注射反应比其他动物更明显，并且反应从一次注射到下一次注射不一致，并随着时间的推移而减少[1]。

在 NHP 中，Remdesivi (静脉注射) 会导致 GS-441524 在血清中的浓度在 7 天的治疗过程中比 Remdesivi 高 1000 倍[3]

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 : 83.33 mg/mL (286.10 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	3.4334 mL	17.1668 mL	34.3336 mL
	5 mM	0.6867 mL	3.4334 mL	6.8667 mL
	10 mM	0.3433 mL	1.7167 mL	3.4334 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, 2 years; -20°C, 1 year。-80°C 储存时，请在 2 年内使用， -20°C 储存时，请在 1 年内使用。

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： 5% Ethanol → 30% Propylene glycol → 45% PEG400 → 20% Water

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	(pH 1.5 with HCl) Solubility: 10 mg/mL (34.33 mM); 澄清溶液; 超声助溶; 酸性条件溶解 (HCl 调节，pH≈2) 方案 二 请依序添加每种溶剂： 5% DMSO → 40% PEG300 → 5% Tween-80 → 50% Saline Solubility: ≥ 2.75 mg/mL (9.44 mM); 澄清溶液 方案 三 请依序添加每种溶剂： 10% DMSO → 40% PEG300 → 5% Tween-80 → 45% Saline Solubility: ≥ 2.08 mg/mL (7.14 mM); 澄清溶液 此方案可获得 ≥ 2.08 mg/mL（饱和度未知）的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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 四 请依序添加每种溶剂： 10% DMSO → 90% (20% SBE-β-CD in Saline) Solubility: ≥ 2.08 mg/mL (7.14 mM); 澄清溶液 此方案可获得 ≥ 2.08 mg/mL（饱和度未知）的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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。 2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。 方案 五 请依序添加每种溶剂： 10% DMSO → 90% Corn Oil Solubility: ≥ 2.08 mg/mL (7.14 mM); 澄清溶液 此方案可获得 ≥ 2.08 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 20.8 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]. Murphy BG, et al. The nucleoside analog GS-441524 strongly inhibits feline infectious peritonitis (FIP) virus in tissue culture and experimental cat infection studies. Vet Microbiol. 2018 Jun;219:226-233. [2]. Katherine Yang, et al. What Do We Know About Remdesivir Drug Interactions? Clin Transl Sci. 2020 May 13;10.1111/cts.12815. [3]. Victoria C. Yan, et al. Advantages of the Parent Nucleoside GS-441524 over Remdesivir for Covid-19 Treatment. ACS Med. Chem. Lett. 2020.

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, 2 years; -20° C, 1 year。-80° C 储存时，请在 2 年内使用， -20° C 储存时，请在 1 年内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
	1 mM	3.4334 mL	17.1668 mL	34.3336 mL	85.8340 mL

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DMSO	**5 mM**	0.6867 mL	3.4334 mL	6.8667 mL	17.1668 mL
	10 mM	0.3433 mL	1.7167 mL	3.4334 mL	8.5834 mL
	15 mM	0.2289 mL	1.1445 mL	2.2889 mL	5.7223 mL
	20 mM	0.1717 mL	0.8583 mL	1.7167 mL	4.2917 mL
	25 mM	0.1373 mL	0.6867 mL	1.3733 mL	3.4334 mL
	30 mM	0.1144 mL	0.5722 mL	1.1445 mL	2.8611 mL
	40 mM	0.0858 mL	0.4292 mL	0.8583 mL	2.1458 mL
	50 mM	0.0687 mL	0.3433 mL	0.6867 mL	1.7167 mL
	60 mM	0.0572 mL	0.2861 mL	0.5722 mL	1.4306 mL
	80 mM	0.0429 mL	0.2146 mL	0.4292 mL	1.0729 mL
	100 mM	0.0343 mL	0.1717 mL	0.3433 mL	0.8583 mL