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产品名称：GAL-021
产品别名：GAL-021

生物活性：

Description	GAL-021 a new intravenous BKCa-channel blocker.
In Vitro	GAL-021 is being developed as a novel breathing control modulator to preserve respiratory drive and protect patients from respiratory impairment due to opioids and other modalities. Using inside-out patches in GH3 cells, GAL-021 exerts concentration-dependent inhibition of single-channel KCa1.1 activity. When evaluated against 12 different cardiac ion channels, inhibition is 35% or less at 30 μM. No significant kinase inhibition is observed at 10 μM. At 30 μM in the radioligand binding assays, interactions (defined as >50% radioligand displacement) are detected at adenosine A1 (65% I), A2A (79% I, IC50 approximately 5μM), and A3 (93% I; IC50 approximately 1 μM) receptors, at 5-HT2B receptors (60% I; IC50 approximately 30 μM)[1].
In Vivo	Intravenously administered GAL-021 attenuates opiate-induced respiratory depression in rats and nonhuman primates without affecting morphine analgesia in rats. GAL-021 ventilatory stimulation in rats is attenuated by carotid sinus nerve transection. GAL-021 ventilatory stimulation is attenuated in mice lacking the pore-forming α-subunit of the KCa 1.1 channel[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 30 mg/mL (117.96 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.9319 mL	19.6595 mL	39.3190 mL
	5 mM	0.7864 mL	3.9319 mL	7.8638 mL
	10 mM	0.3932 mL	1.9659 mL	3.9319 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 (9.83 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (9.83 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 (9.83 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (9.83 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 (9.83 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (9.83 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]. Golder FJ, et al. Identification and Characterization of GAL-021 as a Novel Breathing Control Modulator. Anesthesiology. 2015 Nov;123(5):1093-104.

实验参考：

Animal Administration	Rats: The effects of GAL-021 on mean arterial pressure (MAP) and heart rate (HR) are evaluated using IV infusions. GAL-021 (0.125 mg /kg/min for 25 min, increasing to 0.20 mg/kg/min for an additional 25 min IV) and vehicle (0.9% saline, for 50 min) are administered at a constant infusion rate (6 mL/kg/h). All rats receive additional fluid support (50:50 mixture of lactated Ringer's solution and 6% hetastarch in 0.9% saline at 4 mL/kg/min)[1]. For rat and Mouse Spirometry section, for rats, tracheal airflow is measured using flow spirometry before and after IV (femoral vein) bolus administration of GAL-021 (0.01, 0.03, 0.1, 0.3, 1.0, and 3.0 mg/kg) and vehicle (0.9% saline)[1]. Mice: The effects of GAL-021 on ventilation are also evaluated in age-matched male and female adult $Slo1^{+/+}$ and $Slo1^{-/-}$ mice. Mice are anesthetized using 2 to 2.5% isoflurane in air[1].
Kinase Assay	GAL-021 is dissolved in DMSO, and final assay concentration of DMSO is 0.1% or less. The effects of GAL-021 (30 μM) on a panel of 55 receptors, transporters, and ion channels are evaluated using radioligand binding analyses. Potential kinase inhibition by GAL-021 (10 μM) is assessed using the Kinase HotSpot Screen where activity of 50 kinases is measured in the presence of adenosine triphosphate (10 μM)[1].
References	[1]. Golder FJ, et al. Identification and Characterization of GAL-021 as a Novel Breathing Control Modulator. Anesthesiology. 2015 Nov;123(5):1093-104.