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产品名称：Tonabersat
产品别名：SB-220453；托那博沙

生物活性：

Description	Tonabersat is a gap-junction modulator.
IC_{50} & Target	Gap-junction[1]
In Vitro	Tonabersat, a novel benzopyran derivative, inhibits cortical spreading depression (CSD) and therefore might be able to inhibit the early migraine mechanisms[1].
In Vivo	Treatment with either Tonabersat (10 mg/kg) or Meclofenamate (20 mg/kg) as single agents significantly inhibit progression of metastatic lesions. Addition of carboplatin to either agent profoundly inhibits brain metastasis[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (255.22 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5522 mL	12.7610 mL	25.5219 mL
	5 mM	0.5104 mL	2.5522 mL	5.1044 mL
	10 mM	0.2552 mL	1.2761 mL	2.5522 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 (6.38 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.38 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 (6.38 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (6.38 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

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 (6.38 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.38 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]. Silberstein SD, et al. Tonabersat, a gap-junction modulator: efficacy and safety in two randomized, placebo-controlled, dose-ranging studies of acute migraine. Cephalalgia. 2009 Nov;29 Suppl 2:17-27. [2]. Chen Q, et al. Carcinoma-astrocyte gap junctions promote brain metastasis by cGAMP transfer. Nature. 2016 May 18;533(7604):493-8. [3]. Kim Y, et al. Tonabersat Prevents Inflammatory Damage in the Central Nervous System by Blocking Connexin43 Hemichannels. Neurotherapeutics. 2017 May 30.

实验参考：

Animal Administration	Mice[2] Athymic NCR nu/nu mice, Cr:NIH bg-nu-xid mice, B6129SF1/J, C57BL/6J-*Tmem173gt*/J 'golden ticket', and C57/Bl/6J mice are used at 5-6 weeks of age. For inducible knockdown experiments, mice are given doxycycline hyclate in the drinking water (2 mg/mL) and the diet 14 days after injection of cancer cells. For drug treatment experiments, mice are intraperitoneally injected with Carboplatin (5 mg/kg per 5 days), Tonabersat (MedChem Express) (10 mg/kg per day), or meclofenamic acid sodium salt (20 mg/kg per day). Vehicle (10% DMSO in polyethylene glycol 400) is used in control mice. Quantification of tumour burden is by Bio-luminescent imaging (BLI), performed using an IVIS Spectrum Xenogen instrument and analysed using Living Image software v.2.50.
References	[1]. Silberstein SD, et al. Tonabersat, a gap-junction modulator: efficacy and safety in two randomized, placebo-controlled, dose-ranging studies of acute migraine. Cephalalgia. 2009 Nov;29 Suppl 2:17-27. [2]. Chen Q, et al. Carcinoma-astrocyte gap junctions promote brain metastasis by cGAMP transfer. Nature. 2016 May 18;533(7604):493-8. [3]. Kim Y, et al. Tonabersat Prevents Inflammatory Damage in the Central Nervous System by Blocking Connexin43 Hemichannels. Neurotherapeutics. 2017 May 30.