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产品名称：Paradol
产品别名：姜酮酚；[6]-Gingerone; [6]-Paradol

生物活性：

Description	Paradol is a pungent phenolic substance found in ginger and other Zingiberaceae plants. Paradol is an effective inhibitor of tumor promotion in mouse skin carcinogenesis, binds to cyclooxygenase (COX)-2 active site.
IC_{50} & Target	COX-2
In Vitro	Paradol ([6]-paradol) induces apoptosis in an oral squamous carcinoma cell line, KB, in a dose-dependent manner. Paradol induces apoptosis through a caspase-3-dependent mechanism[2].
In Vivo	Administration of Paradol (6-paradol) (10 mg/kg) clearly reduces the number of Iba1-positive cells 1 and 3 days after the challenge. Moreover, Paradol dramatically reduces the number of Iba1-postive cells in periischemic regions even after 3 days following M/R challenge[3]. Paradol (6-paradol) exhibits the strongest anti-inflammatory effect of several paradol compounds in lipopolysaccharide-stimulated BV2 microglia derived from a mouse brain, including 2-, 4-, 6-, 8-, and 10-paradol. Furthermore, Paradol shows the strongest pungency of all of the known paradol analogues. Paradol also shows the highest contact time at the antiobesity site of action on the basis of the results shown for the absorption of the metabolites in this study[4].

Solvent&Solubility

In Vitro:

DMSO : ≥ 140 mg/mL (502.89 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.5921 mL	17.9604 mL	35.9208 mL
	5 mM	0.7184 mL	3.5921 mL	7.1842 mL
	10 mM	0.3592 mL	1.7960 mL	3.5921 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 (8.98 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (8.98 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 (8.98 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.98 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 (8.98 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.98 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]. van Breemen RB, et al. Cyclooxygenase-2 inhibitors in ginger (Zingiber officinale). Fitoterapia. 2011 Jan;82(1):38-43. [2]. Keum YS, et al. Induction of apoptosis and caspase-3 activation by chemopreventive [6]-paradol and structurally related compounds in KB cells. Cancer Lett. 2002 Mar 8;177(1):41-7. [3]. Gaire BP, et al. Neuroprotective effect of 6-paradol in focal cerebral ischemia involves the attenuation of neuroinflammatory responses in activated microglia. PLoS One. 2015 Mar 19;10(3):e0120203. [4]. Setoguchi S, et al. Pharmacokinetics of Paradol Analogues Orally Administered to Rats. J Agric Food Chem. 2016 Mar 9;64(9):1932-7.

实验参考：

Cell Assay	KB, human oral epidermoid carcinoma cell lines (ATCC CCL-17) are plated at a density of 5×10^3 cells/200 μL/well into 96-well plate. After an overnight growth, the cells are treated with a series of paradol derivatives. All of the derivatives of paradol tested are dissolved in DMSO. The final concentration of DMSO in the culture medium is kept below 0.1% and the controls are treated with DMSO alone. Cell viability is assessed using MTT assay. In brief, after the cells are grown in the media in the absence or presence of the test compounds (e.g., Paradol, 10, 50, 100, 150, and 200 μM) for 48 h, they are then replaced to a 200 μL culture medium containing 0.5 mg/mL MTT for 3 h. The resulting MTT-formazan product is dissolved by an addition of the same volume of DMSO. The amount of formazan is determined by measuring the absorbance at 570 nm[2].
Animal Administration	Mice[3] Male ICR mice (7 weeks old, 36±2 g) challenged with middle cerebral artery occlusion (MCAO)/reperfusion (M/R) are randomly divided into vehicle (10% Tween80)- or Paradol-administered groups (n=6~7 per group). Paradol dissolved in 10% Tween80 is orally administered (10 mg/kg) into mice at 1, 5, or 10 mg/kg immediately after reperfusion. Rats[4] Five-week-old Sprague-Dawley rats (male) are used. At 8 weeks of age, the rats are fasted for 14 h prior to the oral administration of olive oil (1 mL) containing zingerone or 6-, 8-, or 12-paradol (10 mg/kg). Three rats in each group are anesthetized with isoflurane, and samples (0.3 mL) of their blood are collected from their jugular vein using a heparinized needle and syringe at 0 (i.e., prior to

	the oral administration), 0.25, 0.5, 1, 3, 6, and 24 h after the oral administration of the olive oil containing test compounds. The $AUC_{0\text{-}24h}$ values determined using this time schedule are very similar compared with $AUC_{0\text{-}24h}$ that sampled the time points more minutely with other materials in our laboratory.
References	[1]. van Breemen RB, et al. Cyclooxygenase-2 inhibitors in ginger (Zingiber officinale). Fitoterapia. 2011 Jan;82(1):38-43. [2]. Keum YS, et al. Induction of apoptosis and caspase-3 activation by chemopreventive [6]-paradol and structurally related compounds in KB cells. Cancer Lett. 2002 Mar 8;177(1):41-7. [3]. Gaire BP, et al. Neuroprotective effect of 6-paradol in focal cerebral ischemia involves the attenuation of neuroinflammatory responses in activated microglia. PLoS One. 2015 Mar 19;10(3):e0120203. [4]. Setoguchi S, et al. Pharmacokinetics of Paradol Analogues Orally Administered to Rats. J Agric Food Chem. 2016 Mar 9;64(9):1932-7.