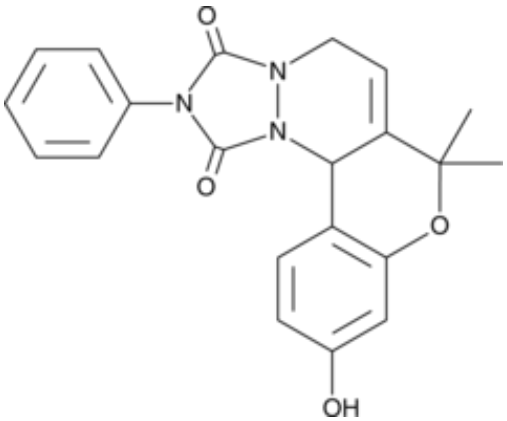
Product Data Sheet

Product Name: Inflachromene
Cat. No.: GC40924

Chemical Properties

Cas. No.	908568-01-4		
Chemical Name	5,12b-dihydro-10-hydroxy-7,7-dimethyl-2-phenyl-1H,7H-[1]benzopyrano[4,3-c][1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione		
SMILES	OC1=CC(OC(C)(C)C2=CCN(C(N(C3=CC=CC=C3)C4=O)=O)N4C25)=C5C=C1		
Formula	$C_{21}H_{19}N_3O_4$	M.Wt	377.4
Solubility	DMF: 30 mg/ml DMSO: 30 mg/ml DMSO:PBS(pH 7.2) (1:4): 0.20 mg/ml Ethanol: 1 mg/ml	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Product Data Sheet

Cell lines	VSMC cells
Preparation Method	Cell viability was measured using cell counting kit-8 (CCK-8, Dojindo) in order to choose suitable Inflachromene concentrations. For the viability assay, VSMCs were pretreated with Inflachromene (5, 10, 15, and 20μM) for 24h.
Reaction Conditions	5, 10, 15, and 20μM; 24h
Applications	Inflachromene dramatically decreased Ang II–induced VSMC proliferation.

Animal experiment [2]:

Animal models	PTZ-induced seizure model
Preparation Method	PTZ induced seizure model was conducted. Stainless steel screws were screwed into the dorsal aspect of the anterior fontanelle, the bilateral sensory cortex and the ventral aspect of the posterior fontanelle, and fixed with dental cement. The anterior and posterior screws were used as cortical EEG recording and grounding, respectively. Mice were treated with 3 and 10mg/kg Inflachromene or vehicle 15 minutes before the injection of PTZ (80mg/kg, ip).
Dosage form	3 and 10mg/kg; ip; single injection
Applications	Inflachromene alleviates the severity of PTZ-induced seizures in a dose-dependent manner.

Caution: Product has not been fully validated for medical applications. For research use only.
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References:
[1]. Liang J, Zbieg JR, Blake RA, et al. GDC-9545 (Giredestrant): a potent and orally bioavailable selective estrogen receptor antagonist and degrader with an exceptional preclinical profile for ER+ breast cancer. Journal of Medicinal Chemistry. 2021 Jul 12; 64(16): 11841-11846.
[2]. Dai SJ, Shao YY, Zheng Y, et al. Inflachromene attenuates seizure severity in mouse epilepsy models via inhibiting HMGB1 translocation. Acta Pharmacologica Sinica. 2023 Sep; 44(9): 1737-1747.

Background

Inflachromene is an inhibitor of HMGB1 and HMGB expression. Inflachromene can inhibit the release of HMGB1 and the NF-κB signaling pathway, exerting anti-inflammatory and neuroprotective effects. Inflachromene is mainly used to treat epilepsy [1-4].

In VSMC cells, Inflachromene (5, 10, 15, and 20μM, 24h) dramatically decreased Ang II–induced VSMC proliferation [5]. In HEK293T cells, Inflachromene (25 and 50μM, 6h) dramatically decreased the endogenous Beclin 1 protein level in a dose- and time-dependent manner whereas the levels of ATG5–ATG12 conjugate, ATG7 and ATG16L1 were not changed [6]. Inflachromene (10μM, 6d) induces senescence rapidly and homogeneously in the popular fetal lung fibroblast (IMR90) cell model, while also constraining SASP production and its paracrine effects [7].

In C57BL/6 mouse, Inflachromene (5 and 10mg/kg, ip, 14d) attenuated the neointimal formation induced by the carotid wire injury in mice [5]. In PTZ-induced seizure model, Inflachromene (3 and 10mg/kg, ip, single injection) alleviates the severity of PTZ-induced seizures in a dose-dependent manner [8]. In sepsis-associated encephalopathy (SAE) mice model, Inflachromene (10mg/kg, ip, 9d) improves cognitive impairment in SAE mice by inhibiting HMGB1-mediated microglial activation, alleviating synaptic damage and neuronal dysfunction [9]. In carbon tetrachloride (CCl_4) induced liver fibrosis mouse model, Inflachromene (10mg/kg, ip, 28d) reduces HMGB2 expression and function and protects mice from liver fibrosis [10].

References:
[1]. Lee S, Nam Y, Koo JY, et al. A small molecule binding HMGB1 and HMGB2 inhibits microglia-

mediated neuroinflammation. Nature chemical biology. 2014 Dec; 10(12): 1055-1060.
[2]. Teng S, Zhu Z, Wu C, et al. Inflachromene inhibits intimal hyperplasia through the HMGB1/2-regulated TLR4-NF-κB pathway. International Immunopharmacology. 2023 Jun 1; 119: 110198.
[3]. Lee HH, Im SH, Ahn S, et al. A validated UPLC-MS/MS method for pharmacokinetic study of inflachromene, a novel microglia inhibitor. Journal of Pharmaceutical and Biomedical Analysis. 2019 Mar 20; 166: 183-188.
[4]. Zhang S, Chen F, Zhai F, et al. Role of HMGB1/TLR4 and IL-1β/IL-1R1 signaling pathways in epilepsy. Frontiers in neurology. 2022 Jun 28; 13: 904225.
[5]. Teng S, Zhu Z, Wu C, et al. Inflachromene inhibits intimal hyperplasia through the HMGB1/2-regulated TLR4-NF-κB pathway. International Immunopharmacology. 2023 Jun 1; 119: 110198.
[6]. Kim YH, Kwak MS, Shin JM, et al. Inflachromene inhibits autophagy through modulation of Beclin 1 activity. Journal of Cell Science. 2018 Feb 15; 131(4): jcs211201.
[7]. Palikyras S, Sofiadis K, Stavropoulou A, et al. Rapid and synchronous chemical induction of replicative-like senescence via a small molecule inhibitor. Aging Cell. 2024 Apr; 23(4): e14083.
[8]. Dai SJ, Shao YY, Zheng Y, et al. Inflachromene attenuates seizure severity in mouse epilepsy models via inhibiting HMGB1 translocation. Acta Pharmacologica Sinica. 2023 Sep; 44(9): 1737-1747.
[9]. Yin XY, Tang XH, Wang SX, et al. HMGB1 mediates synaptic loss and cognitive impairment in an animal model of sepsis-associated encephalopathy. Journal of Neuroinflammation. 2023 Mar 11; 20(1): 69.
[10]. Huang Y, Liangpunsakul S, Rudraiah S, et al. HMGB2 is a potential diagnostic marker and therapeutic target for liver fibrosis and cirrhosis. Hepatology Communications. 2023 Nov 1; 7(11): e0299.

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