Indomethacin

Cat. No.: HY-14397

CAS No.: 53-86-1

Molecular Formula: $C_{19}H_{16}ClNO_4$

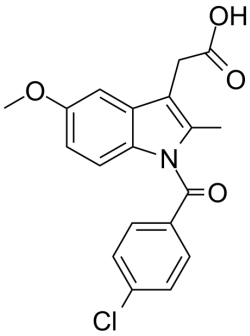
Molecular Weight: 357.79

Target: COX; Autophagy

Pathway: Immunology/Inflammation; Autophagy

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (279.49 mM; Need ultrasonic)

Ethanol : 12.5 mg/mL (34.94 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7949 mL	13.9747 mL	27.9494 mL
5 mM	0.5590 mL	2.7949 mL	5.5899 mL
10 mM	0.2795 mL	1.3975 mL	2.7949 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.81 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.81 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.81 mM); Clear solution
4. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (3.49 mM); Clear solution
5. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (3.49 mM); Clear solution
6. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (3.49 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Indomethacin (Indometacin) is a potent, blood-brain permeable and nonselective inhibitor of COX1 and COX2, with IC_{50}s of 18 nM and 26 nM for human COX-1 and COX-2, respectively, in CHO cells[1]. Indomethacin disrupts autophagic flux by disturbing the normal functioning of lysosomes[2].
IC_{50} & Target	Human COX-1 18 nM (IC_{50}, in CHO cells) Human COX-2 26 nM (IC_{50}, in CHO cells)
In Vitro	Indomethacin is a potent and nonselective inhibitor of COX1 and COX2, with IC_{50}s of 18 nM and 26 nM for human COX-1 and COX-2, respectively, in CHO cells. Indomethacin inhibits lipopolysaccharide (LPS)-induced PGE2 production (COX-2) in a human whole blood assay with a potency (IC_{50}=0.68±0.17 μM), and suppresses coagulation-induced TXB2 production (COX-1) (IC_{50}=0.19±0.02 μM). Indomethacin blocks COX-1 with an IC_{50} of 20±1 nM in U937 cell microsomes at a low arachidonic acid concentration (0.1 μM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Indomethacin dose-dependently inhibits both the carrageenan-induced rat paw oedema (ED_{50}, 2.0 mg/kg), hyperalgesia (ED_{50}, 1.5 mg/kg), and is also effective at reversing LPS-induced pyrexia in rats (ED_{50}, 1.1 mg/kg)[1]. Indomethacin (2.5 mg/kg, i.p) decreases the number of $NeuN^+$ cells in the animals at 8 days after ET-1 injection. Indomethacin also reduces microglia/macrophage activation at 14 days. Indomethacin significantly increases the number of SVZ DCX^+ cells/field at 14 days post stroke[3]. Indomethacin (22.9 mg/kg, p.o.) produces 8 to 10 linear mucosal lesions extended from the fundic to pyloric area of stomach wall[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [3]	Rats[3] To investigate the effects of Indomethacin treatment on both microglia activation, neuroprotection and adult neurogenesis, rats are divided in four experimental groups: animals injected with ET-1, treated with sterile saline (i.p.) for 7 days and perfused at 8 days following ET-1 injection (group 1, n=4); animals injected with ET-1, treated with Indomethacin (2.5 mg/kg, i.p) for 7 days and perfused at 8 days following ET-1 injection (group 2, n=4); animals injected with ET-1, treated with sterile saline (i.p.) for 7 days and perfused at 14 days following ET-1 injection (group 3, n=4); animals injected with ET-1, treated with Indomethacin (2.5 mg/kg, i.p) for 7 days and perfused at 14 days following ET-1 injection (group 4, n=4). After survival times of 7 or 14 days, animals are deeply anesthetized with a mixture of ketamine hydrochloride (72 mg/kg, i.p.) and xylazine hydrochloride (9 mg/kg, i.p.). After the verification of complete absence of both the corneal and the paw withdraw reflexes, the animals are transcardially perfused with heparinized 0.9% warm phosphate-buffered saline (PBS) followed by 4% cold paraformaldehyde in 0.1 M phosphate buffer (PB), pH 7.4. Brains are post-fixed for 24 h in the same fixative and cryoprotected in different gradients of sucrose-glycerol solutions over 7 days. The tissue is then frozen in an embedding medium, and cut at 30 μM in the coronal plane using a cryostat. Sections are then mounted onto gelatinized slides and stored in a freezer at -20°C[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Chem Mater. 2017, 29(19):8221-8238.
- Clin Transl Med. 2021 Oct;11(10):e548.
- J Med Chem. 2021 Feb 23.
- Eur J Med Chem. 8 August 2021, 113743.
- Int J Nanomedicine. 2020 May 1;15:3087-3098.

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REFERENCES

[1]. Riendeau D, et al. Biochemical and pharmacological profile of a tetrasubstituted furanone as a highly selective COX-2 inhibitor. Br J Pharmacol. 1997 May;121(1):105-17.

[2]. Lopes RS, et al. Indomethacin treatment reduces microglia activation and increases numbers of neuroblasts in the subventricular zone and ischaemic striatum after focal ischaemia. J Biosci. 2016 Sep;41(3):381-94.

[3]. Afroz S, et al. Concentrated phosphatidic acid in cereal brans as potential protective agents against indomethacin-induced stomach ulcer. J Agric Food Chem. 2016 Aug 26.

[4]. Jorge Vallecillo-Hernández, et al. Indomethacin Disrupts Autophagic Flux by Inducing Lysosomal Dysfunction in Gastric Cancer Cells and Increases Their Sensitivity to Cytotoxic Drugs. Sci Rep. 2018 Feb 26;8(1):3593.

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