Tolmetin sodium dihydrate

Cat. No.: HY-B1489

CAS No.: 64490-92-2

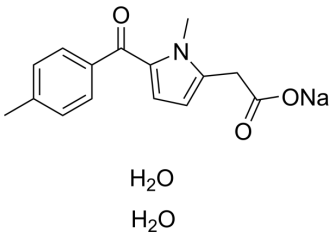
Molecular Formula: $C_{15}H_{18}NNaO_5$

Molecular Weight: 315.3

Target: COX

Pathway: Immunology/Inflammation

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : ≥ 100 mg/mL (317.16 mM)
DMSO : 12.5 mg/mL (39.64 mM; Need ultrasonic)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.1716 mL	15.8579 mL	31.7158 mL
5 mM	0.6343 mL	3.1716 mL	6.3432 mL
10 mM	0.3172 mL	1.5858 mL	3.1716 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 25 mg/mL (79.29 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (3.96 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (3.96 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (3.96 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tolmetin sodium dihydrate is an orally active and potent COX inhibitor with IC_{50}s of 0.35 μM and 0.82 μM human COX-1 and COX-2, respectively. Tolmetin sodium dihydrate is a non-steroidal anti-inflammatory drug (NSAID)[1][2].

IC_{50} & Target

Human COX-1	Human COX-2
0.35 μM (IC_{50})	0.82 μM (IC_{50})

In Vitro	Tolmetin sodium dihydrate (0.25 mM) does not attenuate lipid peroxidation in rat brain homogenate. Tolmetin (0.25, 0.5, 0.75, 1 mM) shows radical scavenging properties but without superoxide anion generation in rat brain homogenat[3]. Tolmetin sodium dihydrate (0.001-100 μM) shows anticancer activity againts HT-29 colon cancer cell line in a dose-dependent manner[4]. Tolmetin sodium dihydrate (0-100 μM) shows no effect on osteoblast growth[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tolmetin sodium dihydrate (30,100 mg/kg; gavage; single dose or twice daily for 3 and 14 days) shows maximal ulcerogenic effect 4 h after the single dose, while potently decreases after 3 and 14 days of repeated administration in male Wistar rats weighing 180-200 g. Tolmetin causes gastric lesions in 100 mg/kg[2]. Tolmetin sodium dihydrate (5 mg/kg twice a day for 5 days) pre-treatment considerably attenuates quinolinic acid (QA)-induced neurotoxicity[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats[1] After 2 weeks of acclimatization, rats are randomized to different groups and given the non-selective COX inhibitors, amtolmetin guacyl (AMG) (50 and 150 mg/kg) and Tolmetin (30 and 100 mg/kg) as well as the selective COX-2 inhibitor, celecoxib (CXIB; 20 and 60 mg/kg). The compounds are suspended in 1% carboxymethylcellulose (CMC) immediately before use and administered by gavage in a 10-mL/kg volume. Control groups receive CMC in the same volume. Rats from each group are divided into 3 subgroups, consisting each of at least 10 animals. Subgroups are dosed either with a single dose (acute treatment group) or twice daily for 3 and 14 days (chronic treatment groups). To ensure that all groups are dosed for the same period of time, those receiving less than 14 days of NSAIDs are given CMC until they are due to start the assigned treatment. Rats are killed by cervical dislocation 4 h after the last administration. Stomachs are immediately removed, opened along the lesser curvature and gently rinsed[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Morini G, et al. Morphological features of rat gastric mucosa after acute and chronic treatment with amtolmetin guacyl: comparison with non-selective and COX-2-selective NSAIDs. Digestion. 2003;68(2-3):124-32. Epub 2003 Nov 7.

[2]. Etcheverry SB, et al. Three new vanadyl(IV) complexes with non-steroidal anti-inflammatory drugs (Ibuprofen, Naproxen and Tolmetin). Bioactivity on osteoblast-like cells in culture. J Inorg Biochem. 2002 Jan 1;88(1):94-100.

[3]. Dairam A, et al. Non-steroidal anti-inflammatory agents, tolmetin and sulindac, attenuate oxidative stress in rat brain homogenate and reduce quinolinic acid-induced neurodegeneration in rat hippocampal neurons. Metab Brain Dis. 2006 Sep;21(2-3):221-33.

[4]. T D Warner, et al. Nonsteroid drug selectivities for cyclo-oxygenase-1 rather than cyclo-oxygenase-2 are associated with human gastrointestinal toxicity: a full in vitro analysis. Proc Natl Acad Sci U S A. 1999 Jun 22;96(13):7563-8.

[5]. DADAŞ, Yakup, et al. Synthesis and anticancer activity of some novel tolmetin thiosemicarbazides. Marmara Pharmaceutical Journal 19(3) • April 2015

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