# Tarenflurbil

**Cat. No.:** HY-10291

**CAS No.:** 51543-40-9

**Molecular Formula:** $C_{15}H_{13}FO_2$

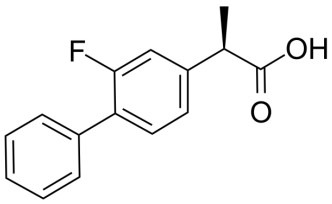
**Molecular Weight:** 244.26

**Target:** RAR/RXR; Autophagy

**Pathway:** Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor; Autophagy

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |




## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : ≥ 50 mg/mL (204.70 mM)

* "≥" means soluble, but saturation unknown.

| Preparing Stock Solutions | Mass / Solvent / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 4.0940 mL | 20.4700 mL | 40.9400 mL |
| | 5 mM | 0.8188 mL | 4.0940 mL | 8.1880 mL |
| | 10 mM | 0.4094 mL | 2.0470 mL | 4.0940 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: ≥ 2.5 mg/mL (10.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (10.23 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (10.23 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Tarenflurbil ((R)-Flurbiprofen) is the R-enantiomer of the racemate NSAID Flurbiprofen, Tarenflurbil ((R)-Flurbiprofen) inhibits the binding of [$^3$H]9-cis-RA to RXRα LBD with $IC_{50}$ of 75 μM. Tarenflurbil can be used for Alzheimer's disease research.

**$IC_{50}$ & Target**

IC50: 75 μM (RXRα)[1]

**In Vitro**

Tarenflurbil ((R)-Flurbiprofen) can significantly reduce Aβ secretion, but at the same time, increases the level of intracellular

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| | Aβ. The binding between [$^3$H]9-cis-RA and RXRα is competitively inhibited by both unlabeled (R)-Flurbiprofen and 9-cis-RA. (R)-Flurbiprofen can interfere with the interaction between RXRα and 9-cis-retinoid acid (9-cis-RA), and that 9-cis-RA decreases Tarenflurbil ((R)-Flurbiprofen)'s reduction of Aβ secretion. Tarenflurbil ((R)-Flurbiprofen) treatment significantly increases the levels of intracellular Aβ species[1]. The well characterized, nonsteroidal anti-inflammatory drug (nonsteroidal anti-inflammatory drug), Tarenflurbil ((R)-Flurbiprofen) affects only Aβ and not Notch β formation, indicating that second generation GSMs and nonsteroidal anti-inflammatory drug-based GSMs have different modes of action regarding Notch processing[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | Effects of the early and late onset of treatment with Tarenflurbil ((R)-Flurbiprofen) are assessed in C57BL6/J mice that develop a non-remitting form of the disease, and in SJL mice that develop a relapsing-remitting (RR)-EAE. Tarenflurbil ((R)-Flurbiprofen) completely prevents the development of clinical EAE scores in C57BL6/J mice when the treatment is started within 3 days after immunization. This regimen is referred to as preventive treatment. The effect is dose-dependent, and the minimum daily dose for complete prevention is 5 mg/kg/day. Effects of Tarenflurbil ((R)-Flurbiprofen) are comparable to those of Fingolimod (FTY720, 0.5 mg/kg/day), which is used as the positive control. Tarenflurbil ((R)-Flurbiprofen) also significantly reduces clinical EAE scores in C57BL6/J mice when treatment is started shortly before onset of clinical manifestations, referred to as semi-therapeutic (10 mg/kg/day) and reduces clinical scores when the treatment is initiated after full development of the disease on day 13 (5 mg/g/day)[3].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

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|---|---|
| **Cell Assay** [2] | HEK293 cells stably expressing human FLAG-Notch1-ΔE (FLAG-NΔE) or APPswe are cultured in Dulbecco's modified Eagle's medium supplemented with 10% fetal bovine serum, nonessential amino acids, 10 μM Hepes, and 300 μg/mL hygromycin or 100 μg/mL Zeocin, respectively. For each experiment, the cells are counted and plated in T75 flasks, 6- or 384-well plates (for Nβ, Aβ, and NICD experiments, respectively) the day before treatment. On the following day, the GSM, Tarenflurbil ((R)-Flurbiprofen) (200 μM), sulindac sulfide (125 μM), AZ1136 (25 μM), AZ4126 (400 nM), or vehicle control ($Me_2SO$) is separately added to fresh cell media and incubated for 24, 16, or 5 h (for Nβ, Aβ, and NICD experiments, respectively) before conditioned media or cells are analyzed[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [3] | Mice[3]<br>Female C57BL6/J and female SJL mice, aged 10-12 weeks at immunization, are used for study of primary progressive EAE and relapsing-remitting EAE, respectively. Mice are housed at 3-5 mice per cage at constant room temperature (21±1°C) under a regular light/dark schedule with light from 7:00 a.m. to 7:00 p.m. Food and water are available ad libitum. Animals are treated orally with Tarenflurbil ((R)-Flurbiprofen), S-Flurbiprofen or vehicle or FTY720 via the drinking water. FTY720 (fingolimod) is used as the positive control at 0.5 mg/kg/day. The therapy is continuous and started on day 3 after immunization for preventive treatment, on day 7-8 to allow for some immune activation for analysis, 4 days before onset of clinical symptoms for semi-therapeutic treatment (C57BL6/J), on day 13 after full development of EAE for late-therapeutic treatment of C57BL6/J mice or after the first peak of the disease 19 days after immunization for late-therapeutic treatment of SJL mice. For late-therapeutic treatment of C57BL6/J mice that have a primary progressive course of the disease and do not recover, ${(R)-Flurbiprofen} or vehicle are administered via drug or vehicle soaked sweet cornflakes to ensure drug, fluid and calories intake during the disease. The animals are accustomed to the cornflakes before the start of the therapy. The evaluation of these different therapeutic paradigms increases the predictability of a potential clinical usefulness of Tarenflurbil ((R)-Flurbiprofen) in human MS. For the"late treatment", mice are allocated pairwise to vehicle and ${(R)-Flurbiprofen} groups according to their clinical scores during the first peak so that the scores are identical in both groups at the onset of treatment. The doses of R-Flurbiprofen are 2.5, 5 and 10 mg/kg in C57BL6/J mice and 5 mg/kg/day for SJL mice. S-Flurbiprofen is used at 10 mg/kg/day. The purity of R- and S-Flurbiprofen is >99.9%, and the stability in drinking water and food is confirmed by LC-MS/MS analyses for up to 7 days at room temperature. After this time, recovery of R-Flurbiprofen is 95.7% and of S-Flurbiprofen 91.5%. The experiments adhered to the guidelines of the Committee for Research and Ethical Issues of the International Association for the Study of Pain (IASP) and to those of GV-SOLAS for animal welfare in science.<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## CUSTOMER VALIDATION

- J Appl Toxicol. 2020 Apr;40(4):470-482.
- Biochem Biophys Res Commun. 2023 Dec 6:692:149356.

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## REFERENCES

[1]. You X, et al. Retinoid X receptor-alpha mediates (R )-flurbiprofen's effect on the levels of Alzheimer's beta-amyloid. J Neurochem. 2009 Oct;111(1):142-9.

[2]. Wanngren J, et al. Second generation γ-secretase modulators exhibit different modulation of Notch β and Aβ production. J Biol Chem. 2012 Sep 21;287(39):32640-50.

[3]. Schmitz K, et al. R-flurbiprofen attenuates experimental autoimmune encephalomyelitis in mice. EMBO Mol Med. 2014 Sep 30;6(11):1398-422.



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