

Product Data Sheet

Product Name: Telmisattan

Cat. No.: GC15023

Chemical Properties

Cas. No. 144701-48-4

Chemical Name 2-[4-[[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl]methyl]phenyl]benzoic acid

SMILES CCCC1=NC2=C(C=C(C=C2N1CC3=CC=C(C=C3)C4=CC=CC=C4C(=O)O)C5=NC6=C(C=CC=C6N5C)C

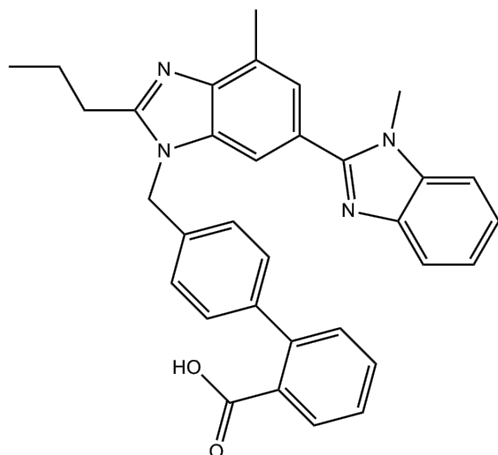
Formula $C_{33}H_{30}N_4O_2$ M.Wt 514.62

Solubility $\geq 9.6\text{mg/mL}$ in DMSO with gentle warming 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]:

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Cell lines	HLF, HLE, HepG2 (poorly differentiated human hepatocellular carcinoma (HCC) cell lines), HuH-7, PLC/PRF/5 (well-differentiated human HCC cell lines) HLF cells were maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 5% fetal bovine serum (FBS) and 100µg/mL penicillin-streptomycin, HLE, HuH-7, PLC/PRF/5 cells were maintained in DMEM supplemented with 10% FBS and penicillin-streptomycin, HepG2 cells were
Preparation Method	maintained in minimum essential medium (MEM) supplemented with 10% FBS and penicillin-streptomycin, all at 37°C, 5% CO₂. For proliferation assay, cells were seeded at 5.0×10³ cells/well in 96-well plates, treated with Telmisattan (0, 10, 50, 100µM) for 48h after 24h adhesion; for cell cycle and related protein detection, HLF cells were treated with 100µM Telmisattan for 12/24/36/48h.
Reaction Conditions	10-100µM; 12-48h
Applications	Telmisattan dose-dependently inhibited the proliferation of poorly differentiated HLF, HLE, HepG2 cells, while the other three ARBs showed no inhibitory effect on HCC cell proliferation, and well-differentiated HuH-7, PLC/PRF/5 cells were insensitive to Telmisattan. For HLF cells, 100µM Telmisattan induced G0/G1 phase arrest, downregulated cyclin D1, cyclin E, CDK4, CDK6, CDK2 expression, increased AMPK (Thr172) phosphorylation and decreased mTOR (Thr2448), p70S6K (Thr389) phosphorylation. Telmisattan partially induced apoptosis in HLF cells, increasing caspase-cleaved cytokeratin 18 level, phosphorylated p53 (Ser392) expression and reducing survivin and phosphorylated ErbB3 levels. Telmisattan altered the miRNA expression profile in HLF cells, upregulating 108 miRNAs (e.g. miR-3651) and downregulating 55 miRNAs (e.g. miR-7-5p), and increased bFGF level in HLF cells.

Animal experiment [2]:

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Animal models	K14-IL-17A ^{ind/+} mice (keratinocyte-specific IL-17A-overexpressing mouse model of severe psoriasis-like skin disease with comorbid hypertension and vascular dysfunction), IL-17A ^{ind/+} littermate control mice
Preparation Method	Mice were administered Telmisattan at 40mg/kg/day via drinking water starting at 6 weeks of age for 4 consecutive weeks; systolic blood pressure was measured by tail-cuff plethysmography, skin disease severity was assessed by modified Psoriasis Area and Severity Index (PASI) scoring every 2 weeks during treatment, then mice were sacrificed for detection of peripheral ROS/RNS formation, plasma cytokine profiles, aortic vasorelaxation response, and aortic Ly6G ⁺ /Ly6C ⁺ neutrophil infiltration.
Dosage form	40mg/kg/day; via drinking water; 4-week continuous treatment
Applications	Telmisattan significantly reduced systolic blood pressure in both K14-IL-17A ^{ind/+} and IL-17A ^{ind/+} control mice, with the systolic blood pressure of Telmisattan-treated K14-IL-17A ^{ind/+} mice comparable to that of Telmisattan-treated control mice. Telmisattan did not lower the elevated peripheral ROS/RNS levels in K14-IL-17A ^{ind/+} mice, did not downregulate the increased plasma levels of IL-17A, G-CSF, IL-6 and IL-1 β in K14-IL-17A ^{ind/+} mice, did not improve the endothelium-dependent aortic relaxation dysfunction in K14-IL-17A ^{ind/+} mice, did not reduce the Ly6G ⁺ /Ly6C ⁺ neutrophil infiltration into the aortic vessel wall of K14-IL-17A ^{ind/+} mice, and did not attenuate the persistent skin inflammation or psoriasis-like lesion PASI score in K14-IL-17A ^{ind/+} mice; Telmisattan treatment also increased the mortality of K14-IL-17A ^{ind/+} mice.

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References:

- [1] Oura K, Tadokoro T, Fujihara S, et al. Telmisartan inhibits hepatocellular carcinoma cell proliferation in vitro by inducing cell cycle arrest. *Oncol Rep.* 2017 Nov;38(5):2825-2835.
- [2] Wild J, Schöler R, Knopp T, et al. Telmisartan Lowers Elevated Blood Pressure in Psoriatic Mice without Attenuating Vascular Dysfunction and Inflammation. *Int J Mol Sci.* 2019 Aug 30;20(17):4261.

Background

Telmisattan is a novel, orally active angiotensin II receptor type 1 (AT1) antagonist ($IC_{50}=9.2nM$). Telmisattan lowers aldosterone by blocking AT1 and partially agonizes PPAR γ to improve metabolism, Telmisattan activates the ACE2/Ang(1-7)/MasR anti-inflammatory pathway to alleviate tissue injury. Telmisattan can be used in research on essential hypertension, metabolic syndrome, and COVID-19^[1-4].

In vitro, Telmisattan (10, 50, 100 μM) was applied to human hepatocellular carcinoma cell lines HLF, HLE, HepG2, HuH-7, and PLC/PRF/5 for 24-48h. Telmisattan dose-dependently inhibited the proliferation of poorly differentiated HLF, HLE, and HepG2 cells. In HLF cells, Telmisattan additionally induced G0/G1 cell cycle arrest, downregulated cyclin D1, cyclin E, CDK4, CDK6, and CDK2 expression, activated AMPK phosphorylation, suppressed mTOR and p70S6K phosphorylation, and induced apoptosis^[5]. Telmisattan (10 μM) was used to pretreat mouse microglial BV2 cells for 2h, followed by LPS (100ng/ml) stimulation for 1h, with a separate Telmisattan-alone group (10 μM ; 3h). Telmisattan alone downregulated the expression of Ccr12, Dusp2, Dusp5, Csfl, Bcl11b, and 11 miRNAs including miR-874 and miR-574 in uninjured BV2 cells, and upregulated Hist1h, Hist2h, Hist4h, Ang4, Slc25a51, and Usp17le (Dub3) genes. Telmisattan pretreatment significantly suppressed the LPS-induced upregulation of pro-injury genes such as IL-1 β , IL-6, TNF α , IkB α , NF- κ B, miR-221, miR-155, TLR2, and Adamts1, and reversed the LPS-induced downregulation of protective genes like snoRNA, Eid2b, Hist1h4m, and Hist1h2bh^[6].

In vivo, Telmisattan (40mg/kg/day) was administered via drinking water to K14-IL-17A^{ind/+} mice with keratinocyte-specific IL-17A overexpression (a psoriasis-like skin disease model) and IL-17A^{ind/+} control mice for 4 consecutive weeks. Telmisattan significantly reduced systolic blood pressure in both K14-IL-17A^{ind/+} and control mice; Telmisattan failed to lower the elevated peripheral ROS/RNS

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levels or the increased plasma levels of IL-17A, G-CSF, IL-6, and IL-1 β in K14-IL-17A^{ind/+} mice^[7]. Telmisattan (2g/kg mixed into solid-formula diet) was given to C57BL/6J mice with ocular hypertension glaucoma model for 12 weeks, with the right eye serving as the contralateral uninjected control. Telmisattan reduced the loss of optic nerve retinal ganglion cell axons and the increase in axonal degeneration percentage caused by elevated intraocular pressure^[8].

References:

- [1] Imenshahidi M, Roohbakhsh A, Hosseinzadeh H. Effects of telmisartan on metabolic syndrome components: a comprehensive review. Biomed Pharmacother. 2024 Feb;171:116169.
- [2] McClellan KJ, Markham A. Telmisartan. Drugs. 1998 Dec;56(6):1039-44; discussion 1045-6.
- [3] Akhrass PR, McFarlane SI. Telmisartan and cardioprotection. Vasc Health Risk Manag. 2011;7:677-83.
- [4] Moen MD. Telmisartan/amlodipine: single-pill combination in hypertension. Am J Cardiovasc Drugs. 2010;10(6):401-12.
- [5] Oura K, Tadokoro T, Fujihara S, et al. Telmisartan inhibits hepatocellular carcinoma cell proliferation in vitro by inducing cell cycle arrest. Oncol Rep. 2017 Nov;38(5):2825-2835.
- [6] Elkahloun AG, Rodriguez Y, Alaiyed S, et al. Telmisartan Protects a Microglia Cell Line from LPS Injury Beyond AT1 Receptor Blockade or PPAR γ Activation. Mol Neurobiol. 2019 May;56(5):3193-3210.
- [7] Wild J, Schöler R, Knopp T, et al. Telmisartan Lowers Elevated Blood Pressure in Psoriatic Mice without Attenuating Vascular Dysfunction and Inflammation. Int J Mol Sci. 2019 Aug 30;20(17):4261.
- [8] Hazlewood RJ, Kuchtey J, Wu HJ, et al. Telmisartan Reduces Axon Degeneration in Mice With Experimental Glaucoma. Invest Ophthalmol Vis Sci. 2020 May 11;61(5):51.

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