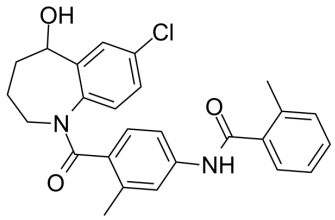
Tolvaptan

Cat. No.:	HY-17000
CAS No.:	150683-30-0
Molecular Formula:	$C_{26}H_{25}ClN_2O_3$
Molecular Weight:	448.94
Target:	Vasopressin Receptor; Autophagy
Pathway:	GPCR/G Protein; 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 : ≥ 100 mg/mL (222.75 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Mass / Solvent / Concentration	1 mg	5 mg	10 mg
1 mM	2.2275 mL	11.1373 mL	22.2747 mL
5 mM	0.4455 mL	2.2275 mL	4.4549 mL
10 mM	0.2227 mL	1.1137 mL	2.2275 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: ≥ 2.17 mg/mL (4.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.17 mg/mL (4.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tolvaptan is a selective, competitive and orally active vasopressin receptor 2 (V_2R) antagonist with an IC_{50} of 1.28 μM for the inhibition of arginine vasopressin (AVP)-induced platelet aggregation. Tolvaptan induces cell apoposis and affects cell cycle. Tolvaptan can be used for the research of hyponatremia[1][2].

In Vitro

Tolvaptan (0-100 μM; 24-168 h) decreases the growth of HepG2 cells[2].
Tolvaptan (20-100 μM; 24-48 h) induces cell death in HepG2 cells[2].
Tolvaptan (0-100 μM; 24-48 h) affects cell cycle of HepG2 cells[2].
Tolvaptan (0-100 μM; 24-48 h) causes DNA damage and induces apoptosis of HepG2 cells[2].
Tolvaptan (0-100 μM; 24-48 h) decreases cyclins and CDKs, and increases γ-H2AX, PARP cleavage and LC3B-II in HepG2 cells

[2].

Tolvaptan (0-100 μM; 4-24 h) induces phosphorylation of JNK, ERK1/2 and p38 in HepG2 cells[2].

Tolvaptan (0-100 μM; 24-28 h) induces autophagy of HepG2 cells[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	HepG2 cells
Concentration:	0-100 μM
Incubation Time:	24, 48, 96 and 168 hours
Result:	Time- and dose-dependently inhibited HepG2 cells with IC_{50}s of ⊠100, 52.2, 33.0 and 27.1 μM at 24, 48, 96 and 168 hours, respectively.

Cell Viability Assay[2]

Cell Line:	HepG2 cells
Concentration:	20, 40, 60, 80, and 100 μM
Incubation Time:	24 and 48 hours
Result:	Time- and dose-dependently inhibited HepG2 cell growth and caused cell death, with LDH released at a concentration over 40 μM. Caused oxidative DNA damage and increased ROS production with a concentration of 60-100 μM.

Cell Cycle Analysis[2]

Cell Line:	HepG2 cells
Concentration:	0-100 μM
Incubation Time:	24 and 48 hours
Result:	Caused cell cycle arrest at the G2 phase, dose-dependently increased the percentage of G0/G1 phase cells with a concentration of 20-60 μM and increased the percentage of G2/M phase cells with a concentration of 60-100 μM.

Western Blot Analysis[2]

Cell Line:	HepG2 cells
Concentration:	0-100 μM
Incubation Time:	24 and 48 hours
Result:	Dose-dependently decreased cyclin D1, cyclin D3, cyclin B1, CDK1, CDK2, CDK4, and CDK6, and increased γ-H2AX which is a maker of DNA double strand breaks in HepG2 cells. Increased the full length PARP into cleavage situation and induced PARP cleavage.

Apoptosis Analysis[2]

Cell Line:	HepG2 cells
Concentration:	0-100 μM
Incubation Time:	24 and 48 hours

Result:	Induced cell apoptosis with increasing caspase 3/7 activity at a dose over 40 μM.

Western Blot Analysis[2]

Cell Line:	HepG2 cells
Concentration:	0-100 μM
Incubation Time:	4 and 24 hours
Result:	Induced the activation of ERK1/2 and p38 after 4 or 24 h of exposure at a concentration over 60 μM in HepG2 cells.

Cell Autophagy Assay[2]

Cell Line:	HepG2 cells
Concentration:	0-100 μM
Incubation Time:	24 and 48 hours
Result:	Induced cell autophagy with autophagosome formation and an increasing lysosomal turnover rate.

In Vivo

Tolvaptan (10 mg/kg; p.o. once per day for 22 days) improves cyclophosphamide (CP)-induced nephrotoxicity in rats[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male albino rats with cyclophosphamide intraperitoneal injection[3]
Dosage:	10 mg/kg
Administration:	Oral gavage; 10 mg/kg once per day; for 22 days
Result:	Improved the level of urine volume, serum Na^+, serum osmolarity, urinary creatinine, free water clearance, serum creatinine, urea, serum K^+, blood pressure, urine osmolarity, fractional excretion of sodium and signs of nephrotoxicity in mice. Decreased caspase-3, Bax and pro-inflammatory cytokines, and increased antiapoptotic Bcl-2 in renal tissue of mice.

CUSTOMER VALIDATION

- J Am Soc Nephrol. 2018 Nov;29(11):2658-2670.
- J Med Chem. 2022 May 17.
- Int J Mol Sci. 2019 Nov 16;20(22):5764.
- Eur J Pharmacol. 2020 Aug 5;880:173157.
- FASEB J. 2019 Jan;33(1):469-483.

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REFERENCES

[1]. Wu Y, et al. Mechanisms of tolvaptan-induced toxicity in HepG2 cells. Biochem Pharmacol. 2015 Jun 15;95(4):324-36.

[2]. El-Shabrawy M, et al. Protective effect of tolvaptan against cyclophosphamide-induced nephrotoxicity in rat models. Pharmacol Res Perspect. 2020 Oct;8(5):e00659.

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