Zuranolone

Cat. No.: HY-103040

CAS No.: 1632051-40-1

Molecular Formula: $C_{25}H_{35}N_3O_2$

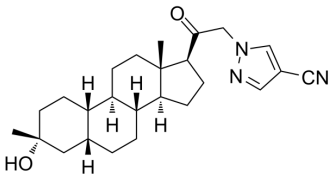
Molecular Weight: 409.56

Target: GABA Receptor

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

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 (244.16 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4416 mL	12.2082 mL	24.4164 mL
5 mM	0.4883 mL	2.4416 mL	4.8833 mL
10 mM	0.2442 mL	1.2208 mL	2.4416 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 (6.10 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.5 mg/mL (6.10 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zuranolone is an orally active and potent neuroactive steroid positive allosteric modulator of $GABA_A$ receptor, with EC_{50}s of 296 and 163 nM for $\alpha_1\beta_2\gamma_2$ and $\alpha_4\beta_3\delta$ $GABA_A$ receptors, respectively[1].

IC_{50} & Target	EC50: 296 nM ($\alpha_1\beta_2\gamma_2$ $GABA_A$ receptor), 163 nM ($\alpha_4\beta_3\delta$ $GABA_A$ receptor)[1]
In Vitro	Zuranolone is a potent $GABA_A$ receptor agonist with EC_{50}s of 296 and 163 nM for $\alpha_1\beta_2\gamma_2$ and $\alpha_4\beta_3\delta$ $GABA_A$ receptors, respectively. Zuranolone is currently being studied in parallel phase 2 clinical trials for the treatment of postpartum depression (PPD) and major depressive disorder (MDD). Zuranolone shows >30 μM inhibition in a cardiac panel of eight relevant cardiac ion channels. At 10 μM concentration of Zuranolone, only binding at the glycine (57%), sigma receptors (88%), and inhibition of the transient receptor potential vanilloid 1 (TRPV1, 95%) is noted[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Acute administration of Zuranolone (0.3 to 10 mg/kg, ip) effectively reduces pentylenetretazol (PTZ)-induced seizures in mice (MEC_{plasma}=85 nM) as well as produces a dose-dependent anticonvulsant effect in the mouse 6 Hz electrical stimulation model. In the rat model of status epilepticus (SE), Zuranolone (0.3 to 5 mg, iv) abolishes both behavioral and electrographic seizure activity, even when administered 60 min after induction of SE. Additional PK studies of Zuranolone in dog show low clearance (<10% of hepatic blood flow), resulting in excellent oral bioavailability (F=68%)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	In vivo pharmacokinetic parameters are determined in male Sprague Dawley rats (of 200 to 300 g in weight), male CD-1 mice (15 to 25 g in weight), and male beagle dogs (8 to 12 kg in weight). Doses of Zuranolone for intravenous (IV) and oral administration (PO) are formulated as solutions in SBECD. Zuranolone is dosed IV (5 mg/kg, 2.5 mL/kg) or by oral gavage (20 mg/kg, 10 mL/kg). Animals in the IV group are sampled at 0.083, 0.25, 1, 2, 4, and 8 hours post-dose and PO animals are sampled at 0.5, 1, 2, 4, and 8 hours post dose. Brain samples from the IV group are also collected at 1 hour post-dose. Blood samples are collected into tubes treated with K2-EDTA, then centrifuged at 2000 g at 4°C for 15 min. Plasma is isolated and frozen at -70°C until extraction[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Biol Chem. 2020 Aug 14;295(33):11495-11512.

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REFERENCES

[1]. Martinez Botella G, et al. Neuroactive Steroids. 2. 3α-Hydroxy-3β-methyl-21-(4-cyano-1H-pyrazol-1'-yl)-19-nor-5β-pregnan-20-one: A Clinical Next Generation Neuroactive Steroid Positive Allosteric Modulator of the (γ-Aminobutyric Acid)A Receptor. J Med Chem. 2017 Sep 28;60(18):7810-7819.

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