Pregnenolone

Cat. No.: HY-B0151

CAS No.: 145-13-1

Molecular Formula: $C_{21}H_{32}O_2$

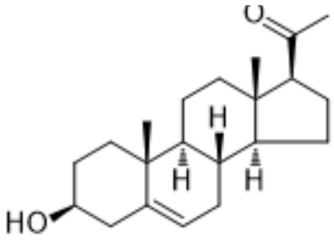
Molecular Weight: 316.48

Target: Cannabinoid Receptor; Autophagy; Endogenous Metabolite; TRP Channel

Pathway: GPCR/G Protein; Neuronal Signaling; Autophagy; Metabolic Enzyme/Protease; Membrane Transporter/Ion Channel

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 : 25 mg/mL (78.99 mM; ultrasonic and warming and heat to 60°C)

H_2O : < 0.1 mg/mL (ultrasonic) (insoluble)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1598 mL	15.7988 mL	31.5976 mL
	5 mM	0.6320 mL	3.1598 mL	6.3195 mL
	10 mM	0.3160 mL	1.5799 mL	3.1598 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (31.60 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 (7.90 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.90 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 1.25 mg/mL (3.95 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Pregnenolone (3β-Hydroxy-5-pregnen-20-one) is a powerful neurosteroid, the main precursor of various steroid hormones including steroid ketones. Pregnenolone acts as a signaling-specific inhibitor of cannabinoid CB1 receptor, inhibits the effects of tetrahydrocannabinol (THC) that are mediated by the CB1 receptors. Pregnenolone can protect the brain from

	cannabis intoxication[1][2]. Pregnenolone is also a TRPM3 channel activator, and also can weakly activate TRPM1 channels[3] .	
IC_{50} & Target	CB1	Human Endogenous Metabolite
In Vitro	CB1 receptor stimulation increases brain Pregnenolone levels, which in turn exerts a negative feedback on the activity of the CB1 receptor antagonizing most of the known behavioral and somatic effects of THC. Pregnenolone likely acts as a signaling-specific negative allosteric modulator binding to a site distinct from that occupied by orthosteric ligands. Pregnenolone does not modify agonist binding but only agonist efficacy[1]. The effect of THC is significantly attenuated when slices are pre-treated with Pregnenolone 100 nM (15.1±1.8 % of inhibition). These effects are likely due to a pre-synaptic action of Pregnenolone. Thus, Pregnenolone blocks the increase in paired-pulse ratio (PPR) induced by THC but does not modify either the amplitude or the decay time of miniature EPSC (mEPSC)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
In Vivo	Pregnenolone administration (2-6 mg/kg) blocks THC-induced food-intake in Wistar rats and in C57BL/6N mice, and blunts the memory impairment induced by THC in mice, but it does not modify these behaviors per se. Injections of Pregnenolone (2 and 4mg/kg) before each self-administration session reduce the intake of WIN 55,212-2 and reduce the break-point in a progressive ratio schedule[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	

PROTOCOL

Animal Administration [1]	Mice and Rats[1] Adult male Wistar rats (weighing 320-340g), Sprague Dawley male rats (weighing 330-350g), C57BL/6N mice (2-3 months) and CD1 mice (weighing 25-30 g at the beginning of the experiments) are used. Pregnenolone is injected subcutaneously (sc) . The injection volumes are 1 mL/kg of body weight for rats and 10 mL/kg for mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Chem Biol. 2022 Aug 18.
- Proc Natl Acad Sci U S A. 2022 Apr 12;119(15):e2117004119.

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REFERENCES

[1]. Vallée M, et al. Pregnenolone can protect the brain from cannabis intoxication. Science. 2014 Jan 3;343(6166):94-8.

[2]. Ducharme N, et al. Brain distribution and behavioral effects of progesterone and pregnenolone after intranasal or intravenous administration. Eur J Pharmacol. 2010 Sep 1;641(2-3):128-34.

[3]. Alan Shiels. TRPM3_miR-204: a complex locus for eye development and disease. Hum Genomics. 2020 Feb 18;14(1):7.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA