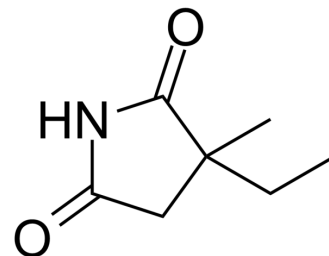


## Ethosuximide

<b>Cat. No.:</b>	HY-B1378		
<b>CAS No.:</b>	77-67-8		
<b>Molecular Formula:</b>	C <sub>7</sub> H <sub>11</sub> NO <sub>2</sub>		
<b>Molecular Weight:</b>	141.17		
<b>Target:</b>	Calcium Channel		
<b>Pathway:</b>	Membrane Transporter/Ion Channel; Neuronal Signaling		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

#### In Vitro

H<sub>2</sub>O : 100 mg/mL (708.37 mM; Need ultrasonic)  
 DMSO : 100 mg/mL (708.37 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	7.0837 mL	35.4183 mL	70.8366 mL
	5 mM	1.4167 mL	7.0837 mL	14.1673 mL
	10 mM	0.7084 mL	3.5418 mL	7.0837 mL

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

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
 Solubility: ≥ 2.08 mg/mL (14.73 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
 Solubility: ≥ 2.08 mg/mL (14.73 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
 Solubility: ≥ 2.08 mg/mL (14.73 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Ethosuximide, a widely prescribed anti-epileptic drug, improves the phenotypes of multiple neurodegenerative disease models and blocks the low voltage activated T-type calcium channel.

#### IC<sub>50</sub> & Target

calcium channel<sup>[1]</sup>

#### In Vitro

The efficacy of Ethosuximide in generalized absence epilepsy is thought to be due to blockade of the low voltage activated

T-type calcium channel. There is no reduction in total Tau levels in Ethosuximide treated Tau transgenic worms as compared to vehicle controls. The rescuing effect of Ethosuximide is therefore not due to transgene suppression or reduced expression of toxic mutant Tau protein. Quantification of the amount of soluble and insoluble (RIPA-extractable) Tau relative to total Tau levels reveals a significant reduction in aberrantly-folded, insoluble Tau and a corresponding increase in soluble Tau in Ethosuximide-treated compared with untreated worms<sup>[1]</sup>. Concentrations of 2  $\mu$ M or more of Ethosuximide not only are found to be less effective than 1  $\mu$ M concentration of Ethosuximide, but also induce cell toxicity. GABA staining immunofluorescence images show that after treatment with Ethosuximide, GABA positive neuron increases by 3 and 6.5 fold for concentrations of 0.1 and 1  $\mu$ M, respectively. BrdU staining shows nuclei proliferation after 2 to 3 days of Ethosuximide exposure. The mean of nuclei is 15.98 $\pm$ 0.41 for the low concentration of Ethosuximide while it is 25.27 $\pm$ 0.48 for the high concentration after BrdU staining. This number is 11.05 $\pm$ 0.2 for lithium chloride<sup>[2]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

### Kinase Assay <sup>[1]</sup>

Vehicle- and Ethosuximide-treated Tau V337M worms are lysed and separated into soluble and insoluble fractions. Fractions are separated by SDS-PAGE and western blotted using anti-human Tau T46 and anti-actin antibodies. The abundance of Tau protein in each fraction is quantified by densitometry and normalized against beta-actin. Total Tau levels in lysates are expressed as the percentage of actin-normalized Tau relative to vehicle control lysates; Tau levels in sequentially extracted fractions are expressed as the percentage of actin-normalized Tau relative to the sum of both fractions (soluble+RIPA) combined<sup>[1]</sup>.

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

### Cell Assay

Neuronal stem cells from the forebrain Cortex of a 3-day-old rat are used in this study. The cells are differentiated by withdrawal of basic fibroblastic growth factor (bFGF) and exposed to Ethosuximide at two concentrations of 0.1  $\mu$ M and 1  $\mu$ M. Before drug treatment, the cells are rinsed once with PBS, and the medium is replaced with fresh, bFGF-free DMEM/F12 medium containing different concentration of Ethosuximide. Medium exchange is done every day for 6 days with medium containing Ethosuximide. Then, cells are fixed for immunocytochemistry<sup>[2]</sup>.

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

## REFERENCES

[1]. Chen X, et al. Ethosuximide ameliorates neurodegenerative disease phenotypes by modulating DAF-16/FOXO target gene expression. *Mol Neurodegener.* 2015 Sep 29;10:51.

[2]. Sondossi K, et al. Analysis of the antiepileptic, ethosuximide impacts on neurogenesis of rat forebrain stem cells. *Fundam Clin Pharmacol.* 2014 Oct;28(5):512-8.

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

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