Enzastaurin

Cat. No.: HY-10342

CAS No.: 170364-57-5

Molecular Formula: $C_{32}H_{29}N_5O_2$

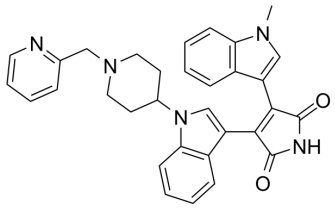
Molecular Weight: 516

Target: PKC; Autophagy; Apoptosis

Pathway: Epigenetics; TGF-beta/Smad; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 8.33 mg/mL (16.14 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9380 mL	9.6899 mL	19.3798 mL
	5 mM	0.3876 mL	1.9380 mL	3.8760 mL
	10 mM	0.1938 mL	0.9690 mL	1.9380 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: ≥ 0.83 mg/mL (1.61 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 0.83 mg/mL (1.61 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Enzastaurin (LY317615) is a potent and selective PKCβ inhibitor with an IC_{50} of 6 nM, showing 6- to 20-fold selectivity over PKCα, PKCγ and PKCε[1].

IC_{50} & Target

PKCβ	PKCα	PKCγ	PKCε
6 nM (IC_{50})	39 nM (IC_{50})	83 nM (IC_{50})	110 nM (IC_{50})

In Vitro

Enzastaurin (LY317615) application results in a marked dose-dependent inhibition of growth in all MM cell lines investigated, including MM.1S, MM.1R, RPMI 8226 (RPMI), RPMI-Dox40 (Dox40), NCI-H929, KMS-11, OPM-2, and U266, with IC_{50} from 0.6-1.6 μM. Enzastaurin direct impacts human tumor cells, inducing apoptosis and suppressing proliferation in cultured tumor cells. Enzastaurin also suppresses the phosphorylation of GSK3βser9, ribosomal protein S6S240/244, and AKTThr308 while having

	no direct effect on VEGFR phosphorylation[1]. Enzastaurin increases apoptosis in malignant lymphocytes of CTCL. When combined with GSK3 inhibitors, enzastaurin demonstrates an enhancement of cytotoxicity levels. Treatment with a combination of enzastaurin and the GSK3 inhibitor AR-A014418 leads to increased levels of β-catenin total protein and β-catenin-mediated transcription. Blocking of β-catenin-mediated transcription or small hairpin RNA (shRNA) knockdown of β-catenin induces the same cytotoxic effects as that of enzastaurin plus AR-A014418. Additionally, treatment with enzastaurin and AR-A014418 decreases the mRNA levels and surface expression of CD44[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Treatment of xenografts with Enzastaurin and radiation produces greater reductions in density of microvessels than either treatment alone. The decrease in microvessel density corresponds to delayed tumor growth[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Induction of apoptosis by enzastaurin is measured by nucleosomal fragmentation and terminal deoxynucleotidyl transferase-mediated nick-end labeling (TUNEL) and staining in HCT116 and U87MG cell lines. Briefly, 5×10^3 cells are plated per well in 96-well plates (1% FBS-supplemented media conditions), incubated with or without Enzastaurin for 48 to 72 hours. The absorbance values are normalized to those from control-treated cells to derive a nucleosomal enrichment factor at all concentrations as per the manufacturer's protocol. The concentrations studied ranges from 0.1 to 10 μM. In situ TUNEL staining is assayed with the In situ Cell Death Detection. Cells (7.5×10^4) are plated per well in 6-well plates and incubated 72 hours in 1% FBS-supplemented media Enzastaurin. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2023 Jun 22;186(13):2929-2949.e20.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Oncogene. 2022 Jan 27.
- NPJ Breast Cancer. 2020 Jan 6;6:1.
- Biochem Pharmacol. 2023 Jan 28;115443.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Rovedo MA, et al. Inhibition of glycogen synthase kinase-3 increases the cytotoxicity of enzastaurin. J Invest Dermatol, 2011, 131(7), 1442-1449.

[2]. Podar K, et al. Targeting PKC in multiple myeloma: in vitro and in vivo effects of the novel, orally available small-molecule inhibitor enzastaurin (LY317615.HCl). Blood, 2007, 109(4), 1669-1677.

[3]. Graff JR, et al. The protein kinase Cbeta-selective inhibitor, Enzastaurin (LY317615.HCl), suppresses signaling through the AKT pathway, induces apoptosis, and suppresses growth of human colon cancer and glioblastoma xenografts. Cancer Res, 2005, 65(16),

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