Parthenolide

Caspase-1 and inflammasome inhibitor

Catalog code: inh-ptd

https://www.invivogen.com/parthenolide

For research use only

Version 20I10-MM

PRODUCT INFORMATION

Contents:

- 50 mg Parthenolide

Storage and stability:

- Product is shipped at room temperature. Upon receipt, store at -20 °C.
- Upon resuspension, prepare aliquots and store at -20 °C. Resuspended parthenolide is stable forat least 6 months when properly stored. Avoid repeated freeze-thaw cycles.

Quality control:

- Purity ≥ 95% (UHPLC)
- The inhibitory activity has been validated using in-house cellular assays.
- The absence of bacterial contamination (e.g. lipoproteins and endotoxins) has been confirmed using HEK-Blue™ TLR2 and HEK-Blue™ TLR4 cells.

DESCRIPTION

Parthenolide is a broad-spectrum inhibitor with numerous anti-inflammatory properties[1]. Its targets include NF-κB, caspase-1, and multiple inflammasomes[1,2]. The inflammasomes are innate immune sensors that drive the activation of inflammatory caspases including caspase-1. They are activated by a two-step process; a first signal ('priming') provided mainly by microbial components or endogenous cytokines involves NF-κB induction, while the second signal provided by a wide array of stimuli including microbial toxins, endogenous molecules or crystalline substances leads to inflammasome assembly and activation. Numerous inflammasomes have been described among them the NLRP3 inflammasome has been best characterized[3].

Notably, this inhibitor blocks the activity of the NLRP1, NLRP3, NLRC4 inflammasomes, but not the AIM2 inflammasome[2, 4, 5]. Mechanistically, it has been reported that parthenolide inhibits the IκB kinase function required for NF-κB activation[6], and alkylates the cysteine residues in caspase-1 and in the ATPase domain of NLRP3, thereby blocking their activity[1,2].

1. Zahid A. *et al.*, 2019. Pharmacological Inhibitors of the NLRP3 Inflammasome. Front Immunol. 2019. 10:2538. **2. Juliana C. *et al.*, 2010.** Anti-inflammatory compounds parthenolide and Bay 11-7082 are direct inhibitors of the inflammasome. J Biol Chem. 285:9792-802. **3. Zheng, D. *et al.*, 2020.** Inflammasome activation and regulation: toward a better understanding of complex mechanisms. Cell Discov 6, 36. **4. Coll R. & O'Neill L., 2011.** The cytokine release inhibitory drug CRID3 targets ASC oligomerisation in the NLRP3 and AIM2 inflammasomes. PLoS One. 6(12): e29539. **5. Honda H. *et al.*, 2014.** Isoliquiritigenin is a potent inhibitor of NLRP3 inflammasome activation and diet-induced adipose tissue inflammation. J Leukoc Biol. 96: 1087-100. **6. Saadane A. *et al.*, 2007.** Parthenolide inhibits IκB kinase, NF-κB activation, and inflammatory response in cystic fibrosis cells and mice. Am J Respir Cell Mol Biol. 36:728-36.

CHEMICAL PROPERTIES

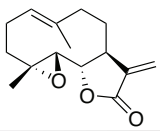
Solubility: 25 mg/ml (101 mM) in DMSO or ethanol

CAS number: 20554-84-1

Formula: $C_{15}H_{20}O_3$

Molecular weight: 248 g/mol

Structure:



METHOD

Preparation of 10 mg/ml (40.4 mM) stock solution

1. Weigh 10 mg of parthenolide.
2. Add 1 ml of DMSO to 10 mg parthenolide. Mix by vortexing.
3. Prepare further dilutions using sterile endotoxin-free water.

***In vitro* inhibition of caspase-1:**

The following protocol describes the monitoring of caspase-1 inhibition in human THP1-Null2 cells by assessing the inhibition of IL-1β production.

1. Prepare a THP1-Null2 cell suspension and add 3 x 10^5 cells per well in a 96-well plate.
2. Prime cells by adding 1 µg/ml LPS-EK for 3 hours at 37 °C in 5% CO_2.
3. Gently remove medium and add fresh test medium.
4. Stimulate cells by adding IL-1β inducers, such as MSU crystals (100-200 mg/ml) in the presence or absence of Parthenolide (0.5-50 µg/ml).
5. Incubate from 6 hours to overnight at 37 °C in 5% CO_2.
6. Determine caspase-1 inhibition by detecting mature IL-1β with InvivoGen's HEK-Blue™ IL-1β cells, which are specifically engineered to detect bioactive IL-1β.

PROTOCOLS

For reference only; as described in the indicated publications.

Cell Culture Assay[1]

Cells: Wild-type bone marrow-derived macrophages
Working concentration: 10 µM (2.5 µg/ml)
Pre-incubation: 15 minutes
Method: *In vitro* caspase-1 activation by SDS-PAGE, followed by immunoblotting with anti-human caspase-1 p30 antibody.

Animal Study[2]

Animal model: Nude nude mice
Dose: 25 mg/kg
Administration: Intraperitoneal injection

RELATED PRODUCTS

Product	Description	Cat. Code
Ac-YVAD-cmk	Caspase -1 inhibitor	inh-yvad
LPS-EK	LPS from *E. coli* K12	tlrl-eklps
MCC950	NLRP3 inflammasome inhibitor	inh-mcc
MSU Crystals	Inflammasome inducer	tlrl-msu
Poly(dA:dT)	Inflammasome inducer	tlrl-patn
THP1-Null2 Cells	Human monocytes	thp-nullz
HEK-Blue™ IL-1β cells	IL-1β reporter cells	hkb-il1b
VX-765	Caspase -1 and -4 inhibitor	inh-vx765i-1

TECHNICAL SUPPORT
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