Semapimod

Cat. No.: HY-15509

CAS No.: 352513-83-8

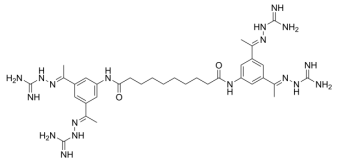
Molecular Formula: $C_{34}H_{52}N_{18}O_2$

Molecular Weight: 744.9

Target: p38 MAPK; Interleukin Related; TNF Receptor

Pathway: MAPK/ERK Pathway; Immunology/Inflammation; Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Semapimod, an inhibitor of proinflammatory cytokine production, can inhibit TNF-α, IL-1β, and IL-6. Semapimod inhibits TLR4 signaling (IC_{50}≈0.3 μM). Semapimod inhibits p38 MAPK and nitric oxide production in macrophages. Semapimod has potential in a variety of inflammatory and autoimmune disorders[1][2][3].

IC_{50} & Target	CD40	IL-1β	IL-6	p38 MAPK

In Vitro

Semapimod leads to a significant decrease of p38-MAPK phosphorylation in macrophages, proinflammatory gene expression of macrophage inflammatory protein-1alpha, interleukin-6, monocyte chemoattractant protein-1, and intercellular adhesion molecule-1, and neutrophil infiltration. Semapimod completely abrogated nitric oxide production within the tunica muscularis[2].

Semapimod desensitizes TLR signaling via its effect on the TLR chaperone gp96. Semapimod tetrahydrochloride inhibits ATP-binding and ATPase activities of gp96 in vitro (IC_{50}≈0.2-0.4 μM). Semapimod desensitizes TLR signaling via its effect on the TLR chaperone gp96[3].

Semapimod (0-500 nM) inhibits microglia-stimulated GL261 invasion[4].

Semapimod (0-10 μM) dose not affect serum-stimulated glioblastoma cell invasion, even at 10 μM, underlining the selectivity of semapimod for cells from the monocytic lineage[4].

Semapimod (200 nM) does not affect microglia-stimulated glioblastoma cell proliferation[4].

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

In Vivo

Semapimod (5 mg/kg; i.p; daily for 2 weeks) ameliorates endothelial dysfunction in Obese Zucker (OZ) rats[1].

Semapimod restores AM-induced akt phosphorylation and cGMP production in OZ rats[1].

Semapimod (6 mg/kg/day, Intracranially for 1 week) inhibits glioblastoma cell invasion in vivo[4].

Semapimod (intracranially administered, 2 weeks) semapimos strongly increases the survival of GL261 tumor-bearing animals in combination with radiation, but has no significant benefit in the absence of radiation[4].

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

Animal Model:	Male OZ rats[1]
Dosage:	5 mg/kg
Administration:	I.p; daily for 2 weeks
Result:	Restored endothelium-dependent vasorelaxation in OZ rats.

Animal Model:	C57Bl/6 mice (GL261 cells were orthotopically implanted)[4]
Dosage:	6 mg/kg/day
Administration:	Intracranially for 1 week, delivered via an osmotic pump
Result:	Inhibited tumor cell invasion by more than 75%.

REFERENCES

[1]. Miller IS, et al. Semapimod sensitizes glioblastoma tumors to ionizing radiation by targeting microglia. PLoS One. 2014 May 9;9(5):e95885.

[2]. Nishimatsu H, et al. Blockade of endogenous proinflammatory cytokines ameliorates endothelial dysfunction in obese Zucker rats. Hypertens Res. 2008;31(4):737-743.

[3]. Wang J, et al. Experimental Anti-Inflammatory Drug Semapimod Inhibits TLR Signaling by Targeting the TLR Chaperone gp96. J Immunol. 2016;196(12):5130-5137.

[4]. Wehner S, Set al. Inhibition of p38 mitogen-activated protein kinase pathway as prophylaxis of postoperative ileus in mice. Gastroenterology. 2009;136(2):619-629.

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