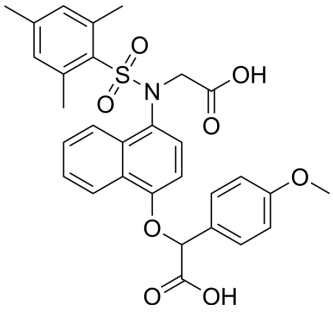
Keap1-Nrf2-IN-14

Cat. No.:	HY-151362
CAS No.:	1928782-31-3
Molecular Formula:	$C_{30}H_{29}NO_8S$
Molecular Weight:	564
Target:	Keap1-Nrf2; Reactive Oxygen Species
Pathway:	NF-κB; Immunology/Inflammation; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Keap1-Nrf2-IN-14 (compound 20c) is a KEAP1-NRF2 inhibitor that effectively disrupts the KEAP1-NRF2 interaction (IC_{50}=75 nM) with a K_d value of 24 nM for KEAP1. Keap1-Nrf2-IN-14 induces the expression of NRF2 target genes and enhances the downstream antioxidant and anti-inflammatory activities. Keap1-Nrf2-IN-14 can be used in the study of oxidative stress-related inflammation[1].

IC_{50} & Target

KEAP1-NRF2
75 nM (IC_{50})

In Vitro

Keap1-Nrf2-IN-14 effectively activated NRF2-ARE regulated cytoprotective defense system in both concentration- and time-dependent manner in RAW264.7 cells[1].
Keap1-Nrf2-IN-14 (1, 10 μM; 12 h) enhanced the antioxidant capacity in macrophage RAW 264.7 cells[1].
Keap1-Nrf2-IN-14 (1, 10 μM; 12 h) attenuates LPS-induced production of inflammation factors in RAW 264.7 cells[1].
Keap1-Nrf2-IN-14 shows high metabolic stability (in co-incubation with rat liver microsomes with half-life of 10.5 h), and have no CYP inhibition on 1A2, 2C9, 2C19, 2D6 and 3A4 when at 10 μM.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	RAW264.7 cells (LPS-stimulated)
Concentration:	10 μM
Incubation Time:	12 h
Result:	Significantly reduced ROS generation to nearly normal level.

Cell Viability Assay[1]

Cell Line:	RAW264.7 cells (LPS-stimulated)
Concentration:	1, 10 μM
Incubation Time:	12 h
Result:	Notably restored the SOD and GSH-Px levels. Markedly attenuated the levels of the inflammatory factors IL-1b, IL-6, TNF-a and NO

	(induced by LPS) in a concentration-dependent manner, and when at 10 μM, almost reduced these cytokines to the basal level.

RT-PCR[1]

Cell Line:	RAW264.7 cells
Concentration:	0.1, 1, 5, 10 μM
Incubation Time:	12 h
Result:	Strongly increased the transcription of NRF2 regulated genes in RAW264.7 cells at a concentration-dependent manner.

Western Blot Analysis[1]

Cell Line:	RAW264.7 cells
Concentration:	10 μM
Incubation Time:	1, 2, 4, 8, 16, 24 h
Result:	Led to nuclear translocation of NRF2 began within 2 h, maximized at 8 h and subsequently declined after 16 h. Induced NRF2, HO-1, NQO-1 and GCLM protein expression in a time- dependent manner.

In Vivo

Keap1-Nrf2-IN-14 (10 mg/kg; i.p.; single daily for 3 days) reduces the LPS-induced production of the proinflammatory factors in vivo[1].

Keap1-Nrf2-IN-14 (1 mg/kg; i.v.; single) shows half-life of 1.72 h in vivo[1].

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

Animal Model:	Female C57BL/6 mice (18-22 g; LPS-induced inflammation model)[1].
Dosage:	10 mg/kg
Administration:	Intraperitoneal injection; single daily for 3 days.
Result:	Diminished LPS-induced inflammatory response in vivo.

Animal Model:	Female C57BL/6 mice (18-22 g; LPS-induced inflammation model)[1].
Dosage:	1 mg/kg
Administration:	Intravenous injection; single.
Result:	Led to half-life of 1.72 h.

REFERENCES

[1]. Lu M C, et al. Discovery of 2-oxy-2-phenylacetic acid substituted naphthalene sulfonamide derivatives as potent KEAP1-NRF2 protein-protein interaction inhibitors for inflammatory conditions. European Journal of Medicinal Chemistry, 2020, 207: 112734.

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

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