Omaveloxolone

Cat. No.: HY-12212

CAS No.: 1474034-05-3

Molecular Formula: $C_{33}H_{44}F_2N_2O_3$

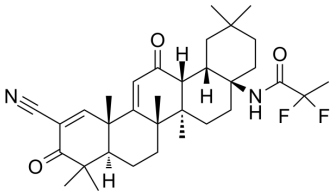
Molecular Weight: 554.71

Target: Keap1-Nrf2; STING; Apoptosis

Pathway: NF-κB; Immunology/Inflammation; Apoptosis

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (180.27 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8027 mL	9.0137 mL	18.0274 mL
	5 mM	0.3605 mL	1.8027 mL	3.6055 mL
	10 mM	0.1803 mL	0.9014 mL	1.8027 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.51 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Omaveloxolone (RTA 408) is an antioxidant inflammation modulator (AIM), which activates Nrf2 and suppresses nitric oxide (NO). Omaveloxolone attenuates osteoclastogenesis by inhibiting STING dependent NF-κb signaling.

IC_{50} & Target

Nrf2[1]

In Vitro

To evaluate the anti-inflammatory activity of Omaveloxolone (RTA 408), RAW 264.7 mouse macrophage cells are treated with Omaveloxolone for two hours and then IFNγ is added to stimulate NO production and release into the media. Omaveloxolone dose-dependently reduces NO concentrations in the media with an IC_{50} value of 4.4±1.8 nM. The potency of Omaveloxolone in this assay is similar to that of Bardoxolone methyl, which has an IC_{50} value of 1.9±0.8 nM. Nrf2 activation is required for AIM-mediated NO suppression. A decrease in nitric oxide synthase 2 (Nos2) protein levels is observed in bardoxolone methyl-treated RAW 264.7 cells, which is attenuated when Nrf2 mRNA levels are reduced by siRNA. To evaluate the anticancer activity of Omaveloxolone, a panel of eight human cell lines derived from tumors of different origin are

	treated with Omaveloxolone and measured cell growth 72 hours later using the sulforhodamine B (SRB) assay. Omaveloxolone inhibits the growth of all tumor lines with an average GI_{50} value of 260±74 nM. To determine whether Omaveloxolone induces apoptosis, the panel of tumor cells are treated with Omaveloxolone and the caspase substrate, DEVD-AFC, for 24 hours. Omaveloxolone dose-dependently increases DEVD-AFC cleavage, indicating that Omaveloxolone treatment triggers caspase activation in cancer cells. Caspase-3 and caspase-9 cleavage is also observed by western blot at the same concentrations of Omaveloxolone that increases DEVD-AFC cleavage[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	To determine whether Omaveloxolone (RTA-408) is an effective mitigator of hematopoietic acute radiation syndrome after bone marrow-lethal doses of total-body irradiation (TBI), mice are administered 3 daily injections of 17.5 mg/kg Omaveloxolone beginning 24 h after TBI. Teatment with Omaveloxolone results in the 35 day survival of 100% of 7 Gy ($LD_{40/35}$) TBI mice ($P<0.05$) and 60% of 7.5 Gy ($LD_{100/13}$) TBI mice ($P<0.0001$)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	MEFs, PANC-1, A549, A375, A549/NF-κB-Luc and HeLa/NF-κB-Luc cells are cultured in Gibco high glucose DMEM with 10% FBS. G-361 cells are cultured in McCoy's 5A medium with 10% FBS. All other cell lines are cultured in RPMI 1640 medium with 10% FBS. For growth inhibition assays, cells are plated in duplicate 96-well culture dishes at 3×10^3 cells per well. The following day, one plate is treated with Omaveloxolone (200, 400, 600, 800 and 1000 nM) and the other is immediately processed for the sulforhodamine B (SRB) assay (time 0). Cells in the Omaveloxolone-treated plate are processed for the SRB assay 72 hours after the start of treatment. Percentage of growth relative to vehicle-treated cells is calculated. Dose-response curves are plotted in GraphPad Prism and GI_{50} values are calculated. For cell counting experiments, MEFs are plated in 6-well culture dishes at 5×10^4 cells per well and treated with Omaveloxolone the following day. Following treatment, cells are counted using a Vi-CELL XR cell analyzer. For clonogenic assays, wild-type (1×10^3 cells per well) and $Keap1^{-/-}$ (0.5×10^3 cells per well) MEFs are seeded in 6-well dishes. Six hours later, MEFs are treated with Omaveloxolone. After seven days, colonies are fixed with a 1:7 solution of acetic acid:MeOH and stained with 0.5% crystal violet in MeOH. Colonies consisting of ≥50 cells are counted[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] For radiation survival experiments, wild-type C57Bl/6 CD45.2 mice (6-8 weeks old) are used. Congenic wild-type C57Bl/6 CD45.1 and C57Bl/6 CD45.1/CD45.2 hybrid host mice are used as recipients in transplantation experiments. Omaveloxolone stock solutions for vehicle control (DMSO) are prepared within 1 h before injection. Omaveloxolone (17.5 mg/kg) or DMSO is administered intraperitoneally at 24, 48 and 72 h after irradiation. Whole-body irradiation (7-8 Gy) is performed using a 250-kVp X-ray machine with 50 cm source-to-skin distance and a 2 mm copper filter. The dose rate is approximately 1.4 Gy/min. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Metab. 2021 Jun 1;33(6):1205-1220.e5.
- Redox Biol. 2020 Jan;28:101309.
- Osteoarthritis Cartilage. 2023 May 7;S1063-4584(23)00776-8.
- Antioxidants (Basel). 2023, 12(1), 133.
- Antioxidants (Basel). 2021, 10(9), 1466.

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REFERENCES

[1]. Probst BL, et al. RTA 408, A Novel Synthetic Triterpenoid with Broad Anticancer and Anti-Inflammatory Activity. PLoS One. 2015 Apr 21;10(4):e0122942.

[2]. Goldman DC, et al. The triterpenoid RTA 408 is a robust mitigator of hematopoietic acute radiation syndrome in mice. Radiat Res. 2015 Mar;183(3):338-44

[3]. Peng Han, et al. RTA-408 Protects Kidney from Ischemia-Reperfusion Injury in Mice via Activating Nrf2 and Downstream GSH Biosynthesis Gene. Oxid Med Cell Longev. 24 December 2017.

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