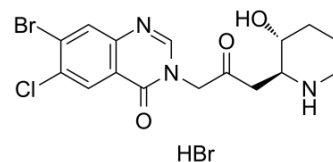


Halofuginone hydrobromide

Cat. No.:	HY-N1584A												
CAS No.:	64924-67-0												
Molecular Formula:	C ₁₆ H ₁₈ Br ₂ ClN ₃ O ₃												
Molecular Weight:	495.59												
Target:	DNA/RNA Synthesis; TGF-beta/Smad; Parasite												
Pathway:	Cell Cycle/DNA Damage; Stem Cell/Wnt; TGF-beta/Smad; Anti-infection												
Storage:	<table border="0"> <tr> <td>Powder</td> <td>-20°C</td> <td>3 years</td> </tr> <tr> <td></td> <td>4°C</td> <td>2 years</td> </tr> <tr> <td>In solvent</td> <td>-80°C</td> <td>6 months</td> </tr> <tr> <td></td> <td>-20°C</td> <td>1 month</td> </tr> </table>	Powder	-20°C	3 years		4°C	2 years	In solvent	-80°C	6 months		-20°C	1 month
Powder	-20°C	3 years											
	4°C	2 years											
In solvent	-80°C	6 months											
	-20°C	1 month											



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (100.89 mM; Need ultrasonic)
H₂O : 2.6 mg/mL (5.25 mM; Need ultrasonic)

Concentration	Mass		
	1 mg	5 mg	10 mg
1 mM	2.0178 mL	10.0890 mL	20.1780 mL
5 mM	0.4036 mL	2.0178 mL	4.0356 mL
10 mM	0.2018 mL	1.0089 mL	2.0178 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (5.04 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (5.04 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (5.04 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Halofuginone hydrobromide (RU-19110 hydrobromide) is a less-toxic form of Febrifugine, which is isolated from the plant *Dichroa febrifuga*^[1]. Halofuginone inhibits prolyl-tRNA synthetase in an ATP-dependent manner with a K_i of 18.3 nM^[2]. Halofuginone is a specific inhibitor of type-I collagen synthesis and attenuates osteoarthritis (OA) by inhibition of TGF-β activity^{[3][4]}.

IC₅₀ & Target

Ki: 18.3±0.5 nM (prolyl-tRNA synthetase)^[2]

In Vitro

Halofuginone competitively inhibits prolyl-tRNA synthetase by occupying both the proline and tRNA-binding pockets of prolyl-tRNA synthetase^[1].
The IC₅₀s of Halofuginone (1, 10, 100, 1000, 10000 nM; 48 hours) are 114.6 and 58.9 nM in KYSE70 and A549 cells, respectively.

The IC₅₀s of Halofuginone (1, 10, 100, 1000 nM; 24 hours) for NRF2 protein are 22.3 and 37.2 nM in KYSE70 and A549 cells, respectively. The IC₅₀ of Halofuginone for global protein synthesis is 22.6 and 45.7 nM in KYSE70 and A549 cells, respectively [1].

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

Cell Viability Assay^[1]

Cell Line:	KYSE70 cells from human oesophageal cancer harbouring a mutation in the NRF2 gene and A549 cells harbouring the KEAP1 gene mutation
Concentration:	1, 10, 100, 1000, 10000 nM
Incubation Time:	48 hours
Result:	The IC ₅₀ s were 114.6 and 58.9 nM in KYSE70 and A549 cells, respectively.

Western Blot Analysis^[1]

Cell Line:	KYSE70 cells from human oesophageal cancer harbouring a mutation in the NRF2 gene and A549 cells harbouring the KEAP1 gene mutation
Concentration:	1, 10, 100, 1000 nM
Incubation Time:	24 hours
Result:	The IC ₅₀ s for NRF2 protein were 22.3 and 37.2 nM in KYSE70 and A549 cells, respectively.

In Vivo

Halofuginone (0.2, 0.5, 1 or 2.5 mg/kg; injected intraperitoneally every other day for 1 month) attenuates progression of OA in anterior cruciate ligament transection (ACLT) mice. Lower concentration (0.2 or 0.5 mg/kg) has minimal effects on subchondral bone and higher concentration (2.5 mg/kg) induces proteoglycan loss in articular cartilage^[3].
Halofuginone (0.25 mg/kg; intraperitoneally injected; every day; 16 days) decreases NRF2 protein levels in tumors. While the tumor volumes do not change substantially between treatments with the vehicle, Halofuginone (0.25 mg/kg, intraperitoneally injected, every day) or cisplatin alone. Combined treatment with Halofuginone and Cisplatin significantly suppresses the tumor volume compared to treatment with Halofuginone or cisplatin alone^[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	3-month-old male C57BL/6J (WT) mice ^[3]
Dosage:	0.2, 0.5, 1 or 2.5 mg/kg
Administration:	Injected intraperitoneally every other day for 1 month
Result:	Attenuated progression of OA in ACLT mice.

Animal Model:	Male nude mice (BALB/C nu/nu mice) (6-8-week) ^[1]
Dosage:	0.25 mg/kg
Administration:	Intraperitoneally injected; every day; 16 days
Result:	The combined treatment with Cisplatin significantly suppressed the tumor volume. NRF2 protein levels in tumors were indeed decreased.

REFERENCES

- [1]. Tsuchida K, et al. Halofuginone enhances the chemo-sensitivity of cancer cells by suppressing NRF2 accumulation. *Free Radic Biol Med.* 2017 Feb;103:236-247.
- [2]. Keller TL, et al. Halofuginone and other Febrifugine derivatives inhibit prolyl-tRNA synthetase. *Nat Chem Biol.* 2012 Feb 12;8(3):311-7.
- [3]. Cui Z, et al. Halofuginone attenuates osteoarthritis by inhibition of TGF- β activity and H-type vessel formation in subchondral bone. *Ann Rheum Dis.* 2016 Sep;75(9):1714-21.
- [4]. Tracy L McGaha, et al. Halofuginone, an inhibitor of type-I collagen synthesis and skin sclerosis, blocks transforming-growth-factor-beta-mediated Smad3 activation in fibroblasts. *J Invest Dermatol.* 2002 Mar;118(3):461-70.
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Caution: Product has not been fully validated for medical applications. For research use only.