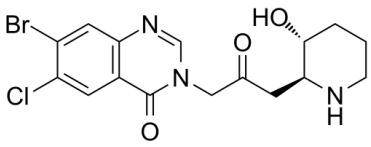
# Data Sheet

| | |
|---|---|
| **Product Name:** | Halofuginone |
| **Cat. No.:** | CS-5485 |
| **CAS No.:** | 55837-20-2 |
| **Molecular Formula:** | $C_{16}H_{17}BrClN_3O_3$ |
| **Molecular Weight:** | 414.68 |
| **Target:** | Calcium Channel; DNA/RNA Synthesis; Parasite; Sodium Channel; TGF-beta/Smad |
| **Pathway:** | Anti-infection; Cell Cycle/DNA Damage; Membrane Transporter/Ion Channel; Neuronal Signaling; Stem Cell/Wnt; TGF-beta/Smad |
| **Solubility:** | DMSO : 20 mg/mL (48.23 mM; ultrasonic and adjust pH to 5 with HCl) |




## BIOLOGICAL ACTIVITY:

Halofuginone (RU-19110), a Febrifugine derivative, is a competitive **prolyl-tRNA synthetase** inhibitor with a **$K_i$** of 18.3 nM[1][2]. Halofuginone is a specific inhibitor of **type-I collagen** synthesis and attenuates osteoarthritis (OA) by inhibition of **TGF-β** activity[3][4]. Halofuginone is also a potent pulmonary vasodilator by activating **Kv channels** and blocking voltage-gated, receptor-operated and store-operated **$Ca^{2+}$ channels**. Halofuginone has anti-malaria, anti-inflammatory, anti-cancer, anti-fibrosis effects[5]. IC50 & Target: Ki: 18.3±0.5 nM (prolyl-tRNA synthetase)[2] **In Vitro:** Halofuginone competitively inhibits prolyl-tRNA synthetase by occupying both the prolineand tRNA-binding pockets of prolyl-tRNA synthetase[1].

The $IC_{50}$s of Halofuginone (1, 10, 100, 1000, 10000 nM; 48 hours) are 114.6 and 58.9 nM in KYSE70 and A549 cells, respectively. The $IC_{50}$s 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 $IC_{50}$ of Halofuginone for global protein synthesis is 22.6 and 45.7 nM in KYSE70 and A549 cells, respectively[1]. Halofuginone increases voltage-gated $K^+$ (Kv) currents in pulmonary artery smooth muscle cells (PASMC) and $K^+$ currents through KCNA5 channels in HEK cells transfected with KCNA5 gene. Halofuginone (0.03-1μM) inhibits receptor-operated $Ca^{2+}$ entry (ROCE) in HEK cells transfected with calcium-sensing receptor gene and attenuated store-operated (SOCE) $Ca^{2+}$ entry in PASMC[5]. **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].

Intraperitoneal administration of Halofuginone (0.3mg/kg, for 2 weeks) partially reverses the established pulmonary hypertension in mice[5].

## 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.

[5]. Pritesh P Jain, et al. Halofuginone, a Promising Drug for Treatment of Pulmonary Hypertension. Br J Pharmacol. 2021 Mar 10.

## CAIndexNames:

4(3H)-Quinazolinone, 7-bromo-6-chloro-3-[3-[(2R,3S)-3-hydroxy-2-piperidinyl]-2-oxopropyl]-, rel-

## SMILES:

O=C1N(CC(C[C@@H]2NCCC[C@H]2O)=O)C=NC3=C1C=C(Cl)C(Br)=C3



Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA