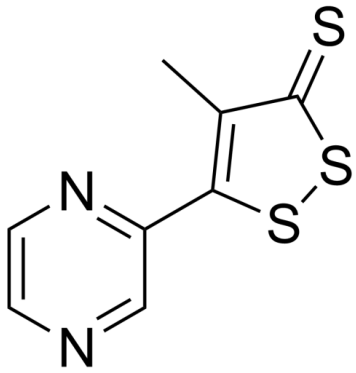
Data Sheet

Product Name:	Oltipraz
Cat. No.:	CS-5412
CAS No.:	64224-21-1
Molecular Formula:	$C_8H_6N_2S_3$
Molecular Weight:	226.34
Target:	HIF/HIF Prolyl-Hydroxylase; HIV; Keap1-Nrf2; Parasite
Pathway:	Anti-infection; Metabolic Enzyme/Protease; NF-κB
Solubility:	DMSO : 6 mg/mL (ultrasonic;warming)



BIOLOGICAL ACTIVITY:

Oltipraz has an inhibitory effect on **HIF-1α** activation in a time-dependent manner, completely abrogating **HIF-1α** induction at ≥10 μM concentrations, the **IC_{50}** of Oltipraz for **HIF-1α** inhibition is 10 μM. Oltipraz is a potent **Nrf2** activator. IC50 & Target: IC50: 10 μM (HIF-1α)[1];

Nrf2[4] ***In Vitro:*** Oltipraz inhibits HIF-1α activity and HIF-1α-dependent tumor growth, which may result from a decrease in HIF-1α stability through S6K1 inhibition in combination with an H2O2-scavenging effect. Oltipraz treatment also inhibits HIF-1α activation stimulated by either hypoxia or CoCl2. Oltipraz is a cancer chemopreventive agent and has an inhibitory effect on angiogenesis and tumor growth. [1] Oltipraz is also a competitive inhibitor of this cytochrome P450, with an apparent Ki of 10 μM. [2] ***In Vivo:*** In wild-type mice, hepatic levels of mRNA for all of the genes analyzed were significantly increased after Oltipraz treatment, with the highest increase (treated/control) for NQO1 mRNA levels (7.6-fold). The Northern blot analyses demonstrated that the observed increases in GST and NQO1 activities by Oltipraz in wild-type mice were preceded by significant elevations in RNA expression. Interestingly, mRNA levels of Nrf2 itself were increased more than 3-fold by Oltipraz treatment. [2]

PROTOCOL (Extracted from published papers and Only for reference)

Enzyme Assay [2] Total GST activity was measured in cytosolic fractions (105,000 × g) in the presence of 0.1% BSA with 1-chloro-2,4-dinitrobenzene as a substrate, whereas NQO1 activity was determined by using menadione as substrate. Protein concentration was determined by the bicinchoninic acid protein assay. Cell assay [1] Hypoxia response element-A549 cell line was established by transfection of hypoxia response element-luciferase reporter plasmid into the human lung carcinoma cell line, A549, using LipofectaminPlus and subsequent selection by treatment with G418 (600 μg/mL; GIBCO). Hypoxia response element-A549 cells were incubated in DMEM. Following overnight serum deprivation, the cells were exposed to 100 nM insulin for 24 h at 37°C with or without 30 μM Oltipraz or each 1,2-dithiole-3-thione congener. Luciferase activity was measured by adding luciferase assay reagent. Animals administration [2] Nrf2-deficient ICR mice were generated. Genotypes of homozygous wild-type and nfr2-deficient mice (7-9 weeks old) were confirmed by PCR amplification of genomic DNA isolated from blood or liver tissue. PCR amplification was carried out by using three different primers, 5′-TGGACGGGACTATTGAAGGCTG-3′ (sense for both genotypes), 5′-CGCCTTTTCAGTAGATGGAGG-3′ (antisense for wild type), and 5′-GCGGATTGACCGTAATGGGATAGG-3′ (antisense for LacZ). To study the effects of nrf2 genotype on induction of phase 2 enzyme activities, female mice (7-9 weeks old) were fed AIN-76A diet and water ad libitum, treated by gavage (0.2 ml) with 500 mg/kg Oltipraz (suspended in 1% cremophor and 25% glycerol) or vehicle only, and killed 48 h later by cervical dislocation. Similarly treated animals were killed 6 and 24 h after treatment to determine the effect of Oltipraz on nuclear localization of Nrf2 and mRNA levels, respectively.

References:

[1]. Lee WH, et al. Oltipraz and dithiolethione congeners inhibit hypoxia-inducible factor-1alpha activity through p70 ribosomal S6 kinase-1 inhibition and H2O2-scavenging effect. Mol Cancer Ther. 2009 Oct;8(10):2791-802.

[2]. Ramos-Gomez M, et al. Sensitivity to carcinogenesis is increased and chemoprotective efficacy of enzyme inducers is lost in nrf2 transcription factor-deficient mice. Proc Natl Acad Sci U S A. 2001 Mar 13;98(6):3410-5.

[3]. Lv S, et al. Glucagon-induced extracellular cAMP regulates hepatic lipid metabolism. J Endocrinol. 2017 Aug;234(2):73-87.

[4]. Eba S, et al.The nuclear factor erythroid 2-related factor 2 activator oltipraz attenuates chronic hypoxia-induced cardiopulmonary alterations in mice.Am J Respir Cell Mol Biol. 2013 Aug;49(2):324-33.

CAIndexNames:

3H-1,2-Dithiole-3-thione, 4-methyl-5-(2-pyrazinyl)-

SMILES:

S=C1SSC(C2=NC=CN=C2)=C1C

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