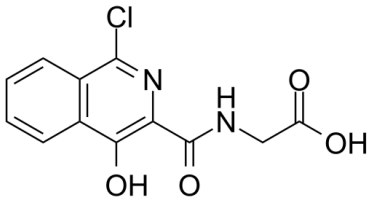
Data Sheet

Product Name:	FG-2216
Cat. No.:	CS-4210
CAS No.:	223387-75-5
Molecular Formula:	C12H9ClN2O4
Molecular Weight:	280.66
Target:	HIF/HIF Prolyl-Hydroxylase
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 31 mg/mL (110.45 mM)



BIOLOGICAL ACTIVITY:

FG-2216 (IOX3; YM311) is a potent HIF-prolyl hydroxylase inhibitor with IC50 of 3.9 uM for PDH2 enzyme; orally bioavailable and induced significant and reversible Epo induction in vivo. IC50 value: 3.9 uM [1] Target: PDH inhibitor FG-2216 was orally bioavailable and induced significant and reversible Epo induction in vivo (82- to 309-fold at 60 mg/kg). Chronic oral dosing in male rhesus macaques was well tolerated, significantly increased erythropoiesis, and prevented anemia induced by weekly phlebotomy. Furthermore, modest increases in HbF-containing red cells and reticulocytes were demonstrated by flow cytometry, though significant increases in HbF were not demonstrated by high-pressure liquid chromatography (HPLC) [2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [2] 1G6 cells are a clonal derivative of Hep3B cells (ATCC, Manassas, VA) and were plated overnight (2.5 × 104 cells/well) in 96-well plates and washed once with Dulbecco modified Eagle medium (DMEM) plus 0.5% FBS prior to incubation with the indicated concentrations of PHIs or vehicle control (0.15% DMSO) for 24 hours. Cell-free culture supernatants were generated by centrifugation of supernatants in a conical-bottom 96-well plate for 5 minutes at 500g. The supernatant was quantitated for epo (R&D Systems, Minneapolis, MN) levels according to the manufacturer's instructions. Animal administration [2] Ten-week-old male Swiss Webster mice (Simonson Labs, Gilroy, CA) were dosed intravenously with the indicated PHI at 60 mg/kg via tail vein. Blood samples were taken under general anesthesia 4 hours after dosing and heparinized plasma was collected. Samples were analyzed for epo by enzyme-linked immunosorbent assay (ELISA; R&D System) according to manufacturer's instructions. Circulating levels of plasma epo were quantitated with a human Epo ELISA kit. Epo values represent the mean plus or minus standard deviation (n = 3 mice/cohort).

References:

[1]. Hong YR, et al. [(4-Hydroxyl-benzo[4,5]thieno[3,2-c]pyridine-3-carbonyl)-amino]-acetic acid derivatives; HIF prolyl 4-hydroxylase inhibitors as oral erythropoietin secretagogues. Bioorg Med Chem Lett. 2013 Nov 1;23(21):5953-7.

[2]. Hsieh MM, et al. HIF prolyl hydroxylase inhibition results in endogenous erythropoietin induction, erythrocytosis, and modest fetal hemoglobin expression in rhesus macaques. Blood. 2007 Sep 15;110(6):2140-7.

CAIndexNames:

Glycine, N-[(1-chloro-4-hydroxy-3-isoquinolinyl)carbonyl]-

SMILES:

O=C(O)CNC(C1=C(O)C2=C(C(Cl)=N1)C=CC=C2)=O

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

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

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