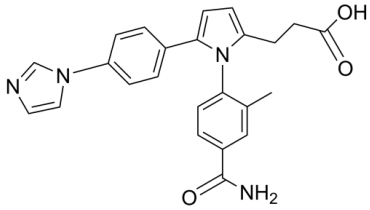
Data Sheet

Product Name:	N6022
Cat. No.:	CS-2034
CAS No.:	1208315-24-5
Molecular Formula:	$C_{24}H_{22}N_4O_3$
Molecular Weight:	414.46
Target:	GSNOR
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 46 mg/mL (110.99 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

N6022 is a potent, selective, reversible, and efficacious **S-Nitrosoglutathione reductase(GSNOR)** inhibitor with **IC_{50}** of 8 nM. IC50 & Target: IC50: 8 nM (GSNOR)[2] ***In Vitro:*** N6022 shows concentration-dependent binding to rat plasma proteins. N6022 has more effect on ATP at lower drug concentrations (20 μM) than on GSH[1]. N6022 binds in the GSNO substrate binding pocket like a competitive inhibitor with an IC_{50} of 8 nM and a K_i of 2.5 nM. N6022 is uncompetitive with cofactors NAD^+ and NADH[2]. ***In Vivo:*** N6022 (50 mg/kg)-treated rats show a slight increase in the incidence of granulomas. In serum, N6022 remains in solution up to 5 mg/mL[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: N6022 is dissolved in 5% DMSO.[1]N6022 is tested using a rat hepatoma (H4IIE) cell line whereby cells are seeded into 96-well plates and cultured in medium containing 20% bovine serum. Following an equilibration period of 48 h, the cells are treated with N6022 (5% DMSO vehicle) at concentrations of 0, 1, 5, 10, 20, 50, 100, and 300 μM for 24 h at 37°C in 5% CO_2. Camptothecin and rotenone are included as positive controls. The cell supernatant or the cells themselves are harvested for biochemical analysis.

References:

[1]. Sun X, et al. Structure-activity relationships of pyrrole based S-nitrosoglutathione reductase inhibitors: pyrrole regioisomers and propionic acid replacement. Bioorg Med Chem Lett. 2011 Jun 15;21(12):3671-5.

[2]. Colagiovanni DB, et al. A nonclinical safety and pharmacokinetic evaluation of N6022: a first-in-class S-nitrosoglutathione reductase inhibitor for the treatment of asthma. Regul Toxicol Pharmacol. 2012 Feb;62(1):115-24.

[3]. Green LS, et al. Mechanism of inhibition for N6022, a first-in-class drug targeting S-nitrosoglutathione reductase. Biochemistry. 2012 Mar 13;51(10):2157-68.

[4]. Thomas M. Raffay, et al. Methods of treating respiratory disorders. Patent. US 20170209419 A1.

CAIndexNames:

1H-Pyrrole-2-propanoic acid, 1-[4-(aminocarbonyl)-2-methylphenyl]-5-[4-(1H-imidazol-1-yl)phenyl]-

SMILES:

OC(CCC1=CC=C(N1C2=CC=C(C(N)=O)C=C2C)C(C=C3)=CC=C3N4C=CN=C4)=O

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

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