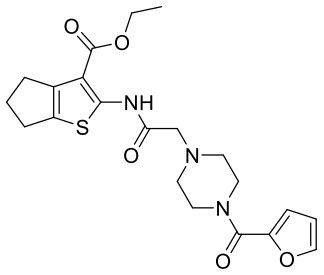
Product data sheet

MedKoo Cat#: 555343 Name: GLX351322 CAS#: 835598-94-2 Chemical Formula: $C_{21}H_{25}N_3O_5S$ Exact Mass: 431.1515 Molecular Weight: 431.51	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
GLX351322 is a NADPH oxidase 4 inhibitor. GLX351322 counteracts glucose intolerance in high-fat diet-treated C57BL/6 mice. GLX351322 inhibits hydrogen peroxide production from tetracycline inducible NOX4-overexpressing cells with IC50 of 5 uM.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	20.0	46.35
DMF	1.0	2.32
DMF:PBS (pH 7.2) (1:2)	0.33	0.76
Ethanol	4.0	9.27

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.32 mL	11.59 mL	23.17 mL
5 mM	0.46 mL	2.32 mL	4.63 mL
10 mM	0.23 mL	1.16 mL	2.32 mL
50 mM	0.05 mL	0.23 mL	0.46 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Liu G, Liu Q, Yan B, Zhu Z, Xu Y. USP7 Inhibition Alleviates H2O2-Induced Injury in Chondrocytes via Inhibiting NOX4/NLRP3 Pathway. Front Pharmacol. 2021 Jan 29;11:617270. doi: 10.3389/fphar.2020.617270. PMID: 33584299; PMCID: PMC7879569.

In vivo study

1. Wu CZ, Li X, Hong L, Han ZN, Liu Y, Wei CX, Cui X. NOX4/Src regulates ANP secretion through activating ERK1/2 and Akt/GATA4 signaling in beating rat hypoxic atria. Korean J Physiol Pharmacol. 2021 Mar 1;25(2):159-166. doi: 10.4196/kjpp.2021.25.2.159. PMID: 33602886; PMCID: PMC7893495.
2. Anvari E, Wikström P, Walum E, Welsh N. The novel NADPH oxidase 4 inhibitor GLX351322 counteracts glucose intolerance in high-fat diet-treated C57BL/6 mice. Free Radic Res. 2015;49(11):1308-18. doi: 10.3109/10715762.2015.1067697. Epub 2015 Jul 30. PMID: 26118714.

7. Bioactivity
Biological target:

Product data sheet

GLX351322 is an inhibitor of NADPH oxidase 4 (Nox4), and inhibits hydrogen peroxide production from NOX4-overexpressing cells with an IC50 of 5 μM.

In vitro activity

oeUSP7 cells and vector control cells were treated with a NOX4 inhibitor (GLX351322, 10 μM) to study NOX4's role in USP7 regulation. Flow cytometry assay showed that inhibition of NOX4 by GLX351322 significantly decreased oeUSP7-induced pyroptosis and ROS production (Figures 5A,B). This study also found that oeUSP7-increased IL-1β and IL-18 were abolished by the inhibition of NOX4 with GLX351322 (Figure 5C). Western blotting results indicated that oeUSP7 resulted in increased expressions of NLRP3, GSDMD-N, active caspase-1, and pro-caspase-1, which was dramatically suppressed by GLX351322 (Figure 5D). These data suggest that USP7 overexpression promotes NLRP3 inflammasome activation and pyroptosis by increasing NOX4.

Reference: Front Pharmacol. 2021 Jan 29;11:617270. https://pubmed.ncbi.nlm.nih.gov/33584299/

In vivo activity

To investigate the effect of hypoxia on NOX2 and NOX4 expression and its role in ANP secretion, a series of experiments were performed using isolated perfused beating rat atria. The results showed that hypoxia significantly upregulated the expression of NOX4 but not NOX2 ($p < 0.05$ vs. control; Fig. 2A and B), which was completely blocked by the ETRA and ETRB antagonists BQ123 and BQ788, respectively ($p < 0.05$ vs. hypoxia; Fig. 2B). In addition, hypoxia-induced ANP secretion was substantially attenuated by the NOX4 antagonist GLX351322 ($p < 0.05$ vs. control and hypoxia, respectively; Fig. 2C). The hypoxia-induced atrial dynamics were shifted to a rightward slightly by GLX351322, but it failed to significantly modulate the inhibitory effect of hypoxia on atrial dynamics ($p < 0.05$ vs. control; Fig. 2D). These results indicate that NOX4 regulated by endogenous ET-1 is involved in the regulation of ANP secretion in beating rat atria under hypoxic conditions.

Reference: Korean J Physiol Pharmacol. 2021 Mar 1; 25(2): 159–166. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7893495/