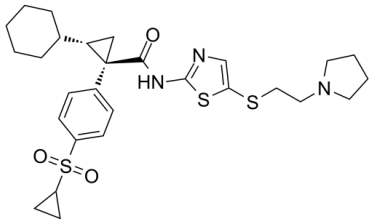
Data Sheet

Product Name:	LY2608204
Cat. No.:	CS-1281
CAS No.:	1234703-40-2
Molecular Formula:	C28H37N3O3S3
Molecular Weight:	559.81
Target:	Glucokinase
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 100 mg/mL (178.63 mM)



BIOLOGICAL ACTIVITY:

LY2608204 is a activator of glucokinase (GK) with EC50 of 42 nM. IC 50 value: 42 nM (EC50) Target: glucokinase in vitro: LY2608204 activates glucokinase (GK) with EC50 of 42 nM at 10 mM glucose with a concentration dependent manner at lower glucose concentrations. LY2608204 also stimulates glucose metabolism in rat insulinoma INS1-E cells with EC50 of 579 nM. in vivo: LY2608204 decreases plasma glucose in a dose-dependent manner at both fasted and postprandial glucose levels. A maximal lowering of glucose AUC versus the untreated control group is observed with the high dose (30 mg/kg) and represents a 42% decrease. Interpolation of the data show that a 20% glucose AUC decrease occurs at an average LY2608204 concentration of 99 ng/mL (179 nM) in plasma, corresponding to a 6.9 mg/kg LY2608204 dose. The in vivo blood brain barrier permeability of LY2608204 results in a mean brain/plasma ratio of 0.17 five minutes post-dose with a mean total brain level of 0.539 nmol/g. Clinical trail:

PROTOCOL (Extracted from published papers and Only for reference)

Kinase assay The human islet GK isoform is expressed in E. coli as (His)6-tagged fusion protein and purified with metal chelate affinity chromatography. After purification the enzyme is stored in aliquots at concentration 0.8 mg/mL in 25 mM sodium phosphate, 150 mM sodium chloride, 100 mM imidazole, 1 mM dithiothreitol, 50% glycerol at -80°C. The assay is performed in flat bottom 96-well plates in a final incubation volume of 100 µL. The incubation mixture consists of 25 mM HEPES (pH7.4), 50 mM potassiumchloride, 2.5 mM magnesiumchloride, 2 mM dithiothreitol, 4 U/mL glucose-6-phosphate dehydrogenase from Leuconostoc mesenteroides, 5 mM ATP, 1 mM NAD and a set concentration of glucose. LY2608204 is dissolved in DMSO and then added to the reaction mixture giving the final DMSO concentration of 10%. The reaction is initiated by addition of 20 µL GK and runs for 20 min at 37°C. The amount of formed NADH is measured as an increase in absorbance at 340 nm using a microplate reader. Absorbance values are used for EC50 calculations.

CAIndexNames:

Cyclopropanecarboxamide, 2-cyclohexyl-1-[4-(cyclopropylsulfonyl)phenyl]-N-[5-[[2-(1-pyrrolidinyl)ethyl]thio]-2-thiazolyl]-, (1R,2S)-

SMILES:

O=C([C@@]1(C2=CC=C(S(=O)(C3CC3)=O)C=C2)[C@H](C4CCCCC4)C1)NC5=NC=C(SCCN6CCCC6)S5

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

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