Product Data Sheet

Product Name: PSN-GK1
Cat. No.: GC31618

Chemical Properties

Cas. No.	745051-61-0		
SMILES	O=C(NC1=NC=C(F)S1)[C@@H](C2=CC=C(S(=O)(C3CC3)=O)C=C2)CC4CCOCC4		
Formula	$C_{20}H_{23}FN_2O_4S_2$	M.Wt	438.54
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	PSN-GK1		

Protocol

Kinase experiment:

Glucokinase activity is measured in a coupled reaction with glucose-6-phosphate dehydrogenase (G6PDH) by monitoring NADPH production at A340 in a plate reader after 15 min incubation at 24°C, in a final volume of 100 µL containing 25 mM HEPES pH 7.1, 25 mM KCl, 5 mM glucose, 1 mM ATP, 2 mM MgCl2, 1 mM DL-dithiothreitol, 1 mM NADP, 2.5 U/mL G6PDH, 0.4 µg GST-glucokinase. Ten dilutions of PSN-GK1 from 0.004 to 100 µM are tested, calculating and fitting fold changes in activity vs controls to sigmoidal curves using a four-parameter logistic model[2].

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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Animal experiment:

Mice[2]C57Bl/6J mice Food is withdrawn 5 h before dosing, while water is available throughout. A blood sample is taken from the tail tip under local anaesthetic for glucose and insulin measurement. Thereafter, mice are weighed and dosed orally with PSN-GK1 (1 or 10 mg/kg) or vehicle. Blood samples are taken 15, 30, 60, 120 and 240 min after dosing, samples (20 µL) for glucose being taken into disposable micro-pipettes and added to 480 µL haemolysis reagent[2].

References:

[1]. Bertram LS, et al. SAR, pharmacokinetics, safety, and efficacy of glucokinase activating 2-(4-sulfonylphenyl)-N-thiazol-2-ylacetamides: discovery of PSN-GK1. J Med Chem. 2008 Jul 24;51(14):4340-5.

[2]. Fyfe MC, et al. Glucokinase activator PSN-GK1 displays enhanced antihyperglycaemic and insulinotropic actions. Diabetologia. 2007 Jun;50(6):1277-87.

Background

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Background

PSN-GK1 is a potent glucokinase activator with an EC50 of 0.13 μM.

PSN-GK1 exhibits an excellent pharmacokinetic profile, with high oral bioavailability, in the rat. PSN-GK1 can markedly reduce blood glucose which accompanied by a trend toward increased pancreatic insulin release. Separately, the antihyperglycemic actions of PSN-GK1 have been shown to be a result of both pancreatic and hepatic effects. In addition, PSN-GK1 engenders potent antihyperglycemic effects in diabetic rodents without causing hypoglycemia[1]. At 5 mM glucose, PSN-GK1 activates glucokinase (4.3-fold, EC50=130 nM), increases MIN6 insulin secretion (26-fold, EC50=267 nM) and 2-DG hepatocytic uptake (3-fold, EC50=1 μM). In C57Bl/6 mice, PSN-GK1 reduces blood glucose at 1 and 10 mg/kg (by mouth), but insulin is increased significantly at only the higher dose. In hyperinsulinaemic 10-mM glucose clamps, PSN-GK1 increases2-DG incorporation into liver glycogen sixfold, directly demonstrating liver effects[2].

[1]. Bertram LS, et al. SAR, pharmacokinetics, safety, and efficacy of glucokinase activating 2-(4-sulfonylphenyl)-N-thiazol-2-ylacetamides: discovery of PSN-GK1. J Med Chem. 2008 Jul 24;51(14):4340-5. [2]. Fyfe MC, et al. Glucokinase activator PSN-GK1 displays enhanced antihyperglycaemic and insulinotropic actions. Diabetologia. 2007 Jun;50(6):1277-87.

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