Product Data Sheet

Product Name: Imeglimin
Cat. No.: GC10576

Chemical Properties

Cas. No.	775351-65-0		
Chemical Name	(4R)-6-N,6-N,4-trimethyl-1,4-dihydro-1,3,5-triazine-2,6-diamine		
SMILES	CC1N=C(NC(=N1)N(C)C)N		
Formula	$C_6H_{13}N_5$	M.Wt	155.2
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	Imeglimin		

Protocol

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Kinase experiment:

Rotenone-sensitive NADH-ubiquinone oxidoreductase (complex I, CI) is assayed using 100 μM Decylubiquinone as an electron acceptor and 200 μM NADH as a donor in a 10 mM KH_2PO_4/K_2HPO_4 buffer, pH 7.5, containing 3.75 mg/mL BSA, 2 mM KCN, and 7.5 μM Antimycin A. NADH oxidation is measured at 340 nm before and after the addition of 4 μM Rotenone to allow the calculation of the Rotenone-sensitive-specific activity, which is characteristic of CI. Succinate-ubiquinone reductase (complex II, CII) activity is quantified by measuring the decrease in absorbance resulting from the reduction of 100 μM dichlorophenolindophenol at 600 nm. The measurement is performed in 50 mM KH_2PO_4/K_2HPO_4 buffer, pH 7.5, in the presence of 30 mM Succinate, 100 μM Decylubiquinone, 2 μM Rotenone, and 2 mM KCN. Coenzyme Q-cytochrome c-oxidoreductase activity (complex III, CIII), is quantified by measuring the increase in absorbance resulting from the reduction of 100 μM cytochrome c at 550 nm. The measurement is performed in 50 mM KH_2PO_4/K_2HPO_4 buffer, pH 7.5, in the presence of 100 μM Decylubiquinone previously reduced by dithionite, 50 μM EDTA, and 1 mM KCN. The specific activity is calculated by subtracting the activity obtained before and after addition of 5 μg/mL Antimycin A. 3-Hydroxyacyl-CoA dehydrogenase (HAD) activity is quantified by measuring the decrease in absorbance at 340 nm resulting from the oxidation of NADH (200 μM) and the reduction of S-acetoacetyl-CoA (50 μM). The measurement is performed in Imidazole (40 mM) and EDTA (60 μM), pH 7[1].

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Animal experiment:

Mice[1]Male C57BL/6JOlaHsd mice at 4 weeks old are housed at 22°C with a 12-h light/dark cycle. After 1 week of acclimatization, 5-6-week-old mice are divided into two groups: one with free access to a standard chow diet (SD) and the other with free access to a pelleted HFHSD diet for 16 weeks. Animals receive Imeglimin 200 mg/kg b.i.d. by oral gavage during the last 6 weeks of HFHSD feeding. Control SD and HFHSD mice are treated by oral gavage with methylcellulose 0.5% as a vehicle for drug treatment (5 mL/kg). Food intake is measured every day during the first week and twice a week until the end of the experiment. Results are expressed as grams per day per mouse.

References:

[1]. Vial G, et al. Imeglimin normalizes glucose tolerance and insulin sensitivity and improves mitochondrialfunction in liver of a high-fat, high-sucrose diet mice model. Diabetes. 2015 Jun;64(6):2254-64.

Background

Imeglimin is the first antidiabetic compound that induces an increase in mitochondrial phospholipid composition, contributing to improvements in hepatic mitochondrial function.

Imeglimin also reduces reactive oxygen species production and increases mitochondrial

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DNA. Imeglimin effects on mitochondrial phospholipid composition can participate in the benefit of Imeglimin on mitochondrial function. Imeglimin increases mtDNA content without modifying PGC1α expression. Imeglimin amplifies the effects of high-fat, high-sucrose diet (HFHSD) on both cardiolipin and phosphatidylserine (PS) content, whereas it tends to restore phosphatidylcholine (PC), phosphatidylethanolamine (PE), and phosphatidylinositol (PI) content to normal values in HFHSD mitochondria[1].

Imeglimin is administered orally at 200 mg/kg b.i.d. during the last 6 weeks of the HFHSD feeding protocol. A slight decrease in body weight and food intake associated with some diarrhea is observed but only during the first few days of treatment. Imeglimin significantly decreases hyperglycemia, restores normal glucose tolerance, and improves insulin sensitivity[1].

References:
[1]. Vial G, et al. Imeglimin normalizes glucose tolerance and insulin sensitivity and improves mitochondrialfunction in liver of a high-fat, high-sucrose diet mice model. Diabetes. 2015 Jun;64(6):2254-64.

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