

Product Data Sheet

Product Name: Metformin HCl

Cat. No.: GC17443

Chemical Properties

Cas. No. 1115-70-4

Chemical Name 3-(diaminomethylidene)-1,1-dimethylguanidine;hydrochloride

SMILES CN(C)C(=N)N=C(N)N.Cl

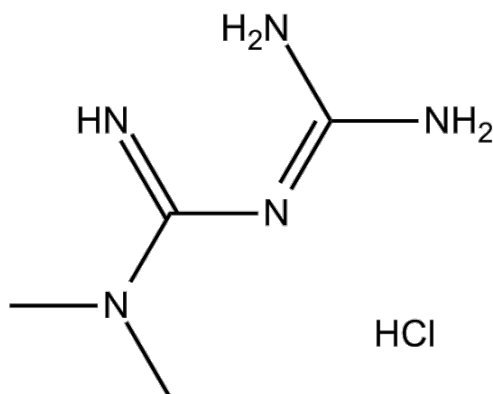
Formula $C_4H_{12}ClN_5$ M.Wt 165.62

Solubility $\geq 8.3\text{mg/mL}$ in DMSO, $\geq 30.7\text{mg/mL}$ in Water Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

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

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Kinase experiment [1]:

AMPK assay

For the AMPK assay, cells were seeded in six-well plates at 1.5×10^6 cells/well in DMEM containing 100 U/ml penicillin, 100 µg/ml streptomycin, 10% FBS, 100 nM insulin, 100 nM dexamethasone, and 5 µg/ml transferrin for 4 hours. Cells were then cultured in serum-free DMEM for 16 hours followed by treatment for 1 hour or 7 hours with control medium, 5-amino-imidazole carboxamide riboside (AICAR), or metformin at concentrations indicated. For a 39-hour treatment, cells for both control and metformin (10 or 20 µM) groups were cultured in DMEM plus 5% FBS and 100 nM insulin, and the fresh control and metformin-containing medium were replaced every 12 hours (last medium change was 3 hours before harvest). After treatment, the cells were directly lysed in digitonin-containing and phosphatase inhibitor-containing buffer A, followed by precipitation with ammonium sulfate at 35% saturation. AMPK activity was determined by measurement of phosphorylation of a synthetic peptide substrate, SAMS (HMRSAMSGHLVKRR).

Cell experiment [1]:

Cell lines

Rat primary hepatocytes

Preparation method

The solubility of this compound in DMSO is limited. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting condition 10, 20, 500 µM, 2 mM; 39h;

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Applications Metformin activated AMPK in primary hepatocytes. Moreover, Metformin (2 mM, 3 hours) stimulated AMPK activity in skeletal muscle in association with induction of glucose uptake. Metformin (500 μ M) reduced hepatic SREBP-1 expression in rat hepatocytes.

Animal experiment:

Animal models Male C57BL/6 mice model;

Dosage form 200 mg/kg, oral gavage, twice daily for 5 days; or 250 mg/kg, intraperitoneal injection, for 3 days

Applications Acetyl-CoA carboxylase (ACC) activity were reduced in metformin-treated rats [1]. Moreover, metformin required LKB1 in the liver to lower blood glucose levels [2].

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

1. Zhou, G., Myers, R., Li, Y., Chen, Y., Shen, X., Fenyk-Melody, J., Wu, M., Ventre, J., Doebber, T., Fujii, N., Musi, N., Hirshman, M. F., Goodyear, L. J. and Moller, D. E. (2001) Role of AMP-activated protein kinase in mechanism of metformin action. J Clin Invest. 108, 1167-1174
2. Shaw, R. J., Lamia, K. A., Vasquez, D., Koo, S. H., Bardeesy, N., Depinho, R. A., Montminy, M. and Cantley, L. C. (2005) The kinase LKB1 mediates glucose homeostasis in liver and therapeutic effects of metformin. Science. 310, 1642-1646

Background

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Metformin HCl is one of the most effective and widely used therapeutics for treatment of type 2 diabetes. It selectively lowers the hepatic gluconeogenesis without rising insulin production, causing weight gain or hypoglycemia. [1]

AMPK (5'AMP-activated protein kinase) acts as a metabolic master switch regulating several intracellular systems including the cellular uptake of glucose, the β -oxidation of fatty acids and the biogenesis of GLUT4 (glucose transporter 4) and mitochondria.

In hepatocytes, AMPK was activated by metformin, followed by decreased ACC (acetyl-CoA carboxylase) activity, induction of fatty acid oxidization and suppression of lipogenic enzyme expression.[2] Metformin also inhibited mGPD (mitochondrial glycerophosphate dehydrogenase), a redox shuttle enzyme, leading to an altered hepatocellular redox state, decreased conversion of lactate and reduced hepatic gluconeogenesis. [1]

In rats treated with metformin, hepatic expression of SEREP-1 mRNAs/protein and activity of ACC were reduced. [2] In metformin treated mice, LKB1 in liver was essential for the ability of metformin to reduce blood glucose [3]. In ASO (Antisense oligonucleotide) knockdown of hepatic mGOD in rats, the phenotype was similar to chronic metformin treatment. It abolished metformin-induced cytosolic redox state, reduction in plasma glucose concentration and EGP inhibition. [1]

References:

1. Madiraju AK, Erion DM, Rahimi Y et al. Metformin suppresses gluconeogenesis by inhibiting mitochondrial glycerophosphate dehydrogenase. Nature. 2014 Jun 26;510(7506):542-6.
2. Zhou G, Myers R, Li Y et al. Role of AMP-activated protein kinase in mechanism of metformin action. J Clin Invest. 2001 Oct;108(8):1167-74.
3. Shaw RJ, Lamia KA, Vasquez D et al. The kinase LKB1 mediates glucose homeostasis in liver and therapeutic effects of metformin. Science. 2005 Dec 9;310(5754):1642-6.

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