

Product Data Sheet

Product Name: Succinyl phosphonate

Cat. No.: GC30030

Chemical Properties

Cas. No. 26647-82-5

SMILES O=C(O)CCC(P(O)(O)=O)=O

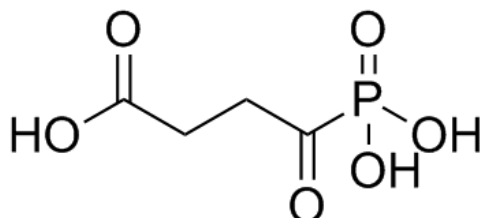
Formula $C_4H_7O_6P$ M.Wt 182.07

Solubility Water : ≥ 50 mg/mL (274.62 mM) 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

Cell experiment [1]:

Cell lines NG108-15 cells

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

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Mus musculus neuroblastoma and Rattus norvegicus glioma hybrid cell line NG108-15 was cultured at 37°C and 5% CO₂ in DMEM with 4.5g/L glucose supplemented with 10% FBS and 100IU/ml penicillin and 100µg/ml streptomycin. OGDHC inhibition and activation treatment was introduced to confluent cells (seeding density 0.5×10^5 cells/cm²), after allowing a 24h period for attachment. During the attachment and treatment period, supplementation with L-glutamine was omitted in order to prevent endogenous production of glutamate from glutamine. Cells were treated with 5mM glutamate, 1mM TH, 0.5mM NO-donor DETA-NONOate and 0.2mM Succinyl phosphonate over 48h. Cell pellets were collected for determination of viability, OGDHC and PDH activity; culture supernatants were collected for detection of extracellular glutamate concentration and LDH release.

Preparation Method

Reaction
Conditions 0.2mM; 48h

Applications Succinyl phosphonate drastically increased the release of LDH induced by glutamate and elevated the levels of resting extracellular glutamate.

Animal experiment [2]:

Animal models male mice

2 to 4-month-old male WT mice were injected with injected with LPS 24h after the intracerebroventricular(icv.) injection of Succinyl phosphonate(1mg/kg body weight) in a volume of 2µL. Control mice were injected with body weight corresponding volumes of saline. 24h after the LPS injection, mice were euthanized, and the brains were extracted and were processed for the following experiments.

Preparation Method

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Dosage form 1mg/kg/day for 24h; icv.

Applications Succinyl phosphonate down-regulated the succinylation levels, reduced ROS production and improved lipid metabolism, and ameliorated MG senescence.

References:

- [1] Weidinger, A., Milivojev, N., Hosmann, A., Duvigneau, J. C., Szabo, C., Törö, G., Rauter, L., Vaglio-Garro, A., Mkrtchyan, G. V., Trofimova, L., Sharipov, R. R., Surin, A. M., Krasilnikova, I. A., Pinelis, V. G., Tretter, L., Moldzio, R., Bay?r, H., Kagan, V. E., Bunik, V. I., & Kozlov, A. V. (2023). Oxoglutarate dehydrogenase complex controls glutamate-mediated neuronal death. *Redox biology*, 62, 102669.
- [2] Zhao, X., Yang, X., Du, C., Hao, H., Liu, S., Liu, G., Zhang, G., Fan, K., & Ma, J. (2024). Up-regulated succinylation modifications induce a senescence phenotype in microglia by altering mitochondrial energy metabolism. *Journal of neuroinflammation*, 21(1), 296.

Background

Succinyl phosphonate is a specific inhibitor of α -ketoglutarate dehydrogenase (α -KGDHC), effective inhibits KGDHC in muscle, bacterial, brain, and cultured human fibroblasts^[1]. α -KGDHC is not only the core enzyme of cellular energy metabolism, but also plays an important role in various physiological processes such as antioxidation and gene expression regulation ^[2]. Succinyl phosphonate is usually used in the research of the mechanisms of oxidative stress and neuroinflammation in neurodegenerative diseases, such Alzheimer's disease and Parkinson's disease ^{[3][4]}.

In vitro, treatment of NG108-15 cells with Succinyl phosphonate (0.2mM) for 48h drastically increased the release of LDH induced by glutamate and elevated the levels of resting extracellular glutamate^[5].

In vivo, intracerebroventricular injection of Succinyl phosphonate(1mg/kg; 24h) in lipopolysaccharide-induced(LPS-induced) microglia mice down-regulated the succinylation levels, reduced ROS

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production and improved lipid metabolism, and ameliorated MG senescence^[6]. Administration of Succinyl phosphonate(0.02mmol/kg; intranasally; 24h) in rats significantly decreased levels of either citrulline or carnosine and increased the activities of OGDHC and malate dehydrogenase^[7].

References:

- [1] Biryukov, A. I., Bunik, V. I., Zhukov, Y. N., Khurs, E. N., & Khomutov, R. M. (1996). Succinyl phosphonate inhibits alpha-ketoglutarate oxidative decarboxylation, catalyzed by alpha-ketoglutarate dehydrogenase complexes from E. coli and pigeon breast muscle. *FEBS letters*, 382(1-2), 167–170.
- [2] Tretter, L., & Adam-Vizi, V. (2005). Alpha-ketoglutarate dehydrogenase: a target and generator of oxidative stress. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences*, 360(1464), 2335–2345.
- [3] Trofimova, L., Lovat, M., Groznaya, A., Efimova, E., Dunaeva, T., Maslova, M., Graf, A., & Bunik, V. (2010). Behavioral impact of the regulation of the brain 2-oxoglutarate dehydrogenase complex by synthetic phosphonate analog of 2-oxoglutarate: implications into the role of the complex in neurodegenerative diseases. *International journal of Alzheimer's disease*, 2010, 749061.
- [4] Sayehmiri, F., Khodagholi, F., Pourbadie, H. G., Naderi, N., Aliakbarzadeh, F., Hashemi, R., Naderi, S., & Motamedi, F. (2022). Phosphonate analog of 2-oxoglutarate regulates glutamate-glutamine homeostasis and counteracts amyloid beta induced learning and memory deficits in rats. *Experimental gerontology*, 168, 111944.
- [5] Weidinger, A., Milivojev, N., Hosmann, A., Duvigneau, J. C., Szabo, C., Törö, G., Rauter, L., Vaglio-Garro, A., Mkrtchyan, G. V., Trofimova, L., Sharipov, R. R., Surin, A. M., Krasilnikova, I. A., Pinelis, V. G., Tretter, L., Moldzio, R., Bayır, H., Kagan, V. E., Bunik, V. I., & Kozlov, A. V. (2023). Oxoglutarate dehydrogenase complex controls glutamate-mediated neuronal death. *Redox biology*, 62, 102669.
- [6] Zhao, X., Yang, X., Du, C., Hao, H., Liu, S., Liu, G., Zhang, G., Fan, K., & Ma, J. (2024). Up-regulated succinylation modifications induce a senescence phenotype in microglia by altering mitochondrial energy metabolism. *Journal of neuroinflammation*, 21(1), 296.
- [7] Bunik, V. I., Artiukhov, A. V., Kazantsev, A. V., Aleshin, V. A., Boyko, A. I., Ksenofontov, A. L., Lukashev, N. V., & Graf, A. V. (2022). Administration of Phosphonate Inhibitors of Dehydrogenases of 2-Oxoglutarate and 2-Oxoadipate to Rats Elicits Target-Specific Metabolic and Physiological Responses. *Frontiers in chemistry*, 10, 892284.

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