

Product Data Sheet

Product Name: Trigonelline

Cat. No.: GN10289

Chemical Properties

Cas. No. 535-83-1

Chemical Name 1-methylpyridin-1-ium-3-carboxylate

SMILES C[N+]1=CC=CC(=C1)C(=O)[O-]

Formula $C_7H_7NO_2$ M.Wt 137.05

Solubility Insoluble in EtOH; ≥ 26 mg/mL in Water; ≥ 8.5 mg/mL in DMSO Storage 4°C, protect from light

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.

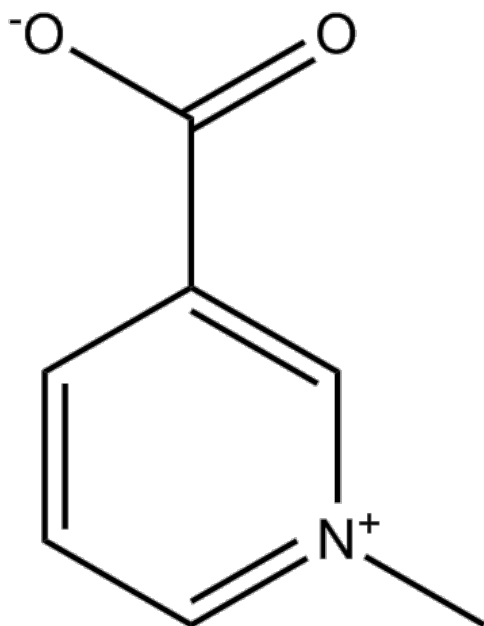
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment [1]:

Cell lines H9c2 cells

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Preparation Method The H9c2 cell line, derived from embryonic BD1X rat heart tissue were cultured in Dulbecco's Modified Eagle's Medium containing 4mM L-glutamine, 4500mg/L glucose, 1mM sodium pyruvate, and 1500mg/L sodium bicarbonate. Cells were treated with different concentration of trigonelline(25-125μM) for 24h and then cells were harvested. The harvested cells were detected with Annexin V-FITC/PI Apoptosis method.

Reaction Conditions 25-125μM; 24h

Applications Trigonelline significantly attenuated H₂O₂-induced cell deaths.

Animal experiment [2]:

Animal models Wild-type C57BL/6 mice

Preparation Method The male, and of wild-type C57BL/6 background 8–10 weeks old were bred in the Specific Pathogen-Free Laboratory Animal Center. The SiO₂-induced fibrosis model involved randomly dividing mice into four groups: (1) PBS+PBS group, (2) PBS+Trigonelline (10mg/kg) group, (3) SiO₂+PBS group, and (4) SiO₂+Trigonelline(10mg/kg) group. SiO₂ (200mg/kg in 50mg/mL PBS) or PBS was administered for endotracheal Perfusion. The starting day of the model was designated as day 1. Starting on day 28, mice in the PBS+Trig (10mg/kg) group and SiO₂+Trigonelline group were administered Trig (10mg/kg) intraperitoneally for 14 consecutive days. Meanwhile, mice in the SiO₂+PBS group and the PBS+PBS group received an equal amount of PBS. On day 42, the mice were euthanized to analyze the pulmonary fibrosis phenotype.

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Dosage form 10mg/kg/day; i.p.; 14 days

Applications Trigonelline reversed silica-induced pulmonary fibrosis, and improved fibrotic pathological features in a silica-induced pulmonary fibrosis mouse model.

References:

- [1] Ilavenil S, Kim DH, Jeong YI, et al. Trigonelline protects the cardiocyte from hydrogen peroxide induced apoptosis in H9c2 cells. *Asian Pac J Trop Med*. 2015;8(4):263-268.
- [2] Zhang F, Yue H, Dong R, et al. Trigonelline hydrochloride attenuates silica-induced pulmonary fibrosis by orchestrating fibroblast to myofibroblast differentiation. *Respir Res*. 2024;25(1):242.

Background

Trigonelline, an alkaloid isolated from *Trigonella foenum-graecum* L or *Leonurus artemisia*, is a potent and specific inhibitor of Nrf2^[1]. Nrf2 (nuclear factor erythroid 2–related factor 2) is the master transcriptional regulator of cellular antioxidant defense, eliminating reactive oxygen species and maintaining redox homeostasis by up-regulating genes such as HO-1 and NQO1^[2]. Trigonelline is widely used in research related to anti-diabetes, anti-oxidation, anti-inflammation and neuroprotection by blocking Nrf2-dependent proteasome activity^{[3][4]}.

In vitro, pretreatment of H9c2 cells with Trigonelline (25-125μM; 24h) before H₂O₂ stimulation significantly rescued cell morphology, attenuated H₂O₂-induced cell deaths, enhanced antioxidant activity, down-regulated the expression of apoptotic genes (caspase-3, caspase-9), and up-regulated the expression of anti-apoptotic genes (Bcl-2, Bcl-XL)^[5]. Trigonelline (0.1-1mM; 16h) significantly inhibited Nrf2 activity in pancreatic cancer cell lines (Panc1, Colo357, MiaPaca2) and H6c7 pancreatic duct cells, reduced nuclear Nrf2 levels and proteasome activity, and enhanced cell sensitivity to tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) and etoposide-induced apoptosis, increasing caspase-3/7 activity by 2.3-4.3 fold^[6].

In vivo, Trigonelline (10mg/kg/day; i.p.; 14 days) reversed silica-induced pulmonary fibrosis, reduced

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the expression of fibrotic markers (such as Collagen 1 and Fibronectin) in lung tissues, inhibited fibroblast-to-myofibroblast differentiation by repressing TGF- β /Smad signaling, and improved fibrotic pathological features in a silica-induced pulmonary fibrosis mouse model^[7].

References:

- [1] Nguyen V, Taine EG, Meng D, Cui T, Tan W. Pharmacological Activities, Therapeutic Effects, and Mechanistic Actions of Trigonelline. *Int J Mol Sci.* 2024;25(6):3385.
- [2] Bellezza I, Giambanco I, Minelli A, Donato R. Nrf2-Keap1 signaling in oxidative and reductive stress. *Biochim Biophys Acta Mol Cell Res.* 2018;1865(5):721-733.
- [3] Ozçelik B, Kartal M, Orhan I. Cytotoxicity, antiviral and antimicrobial activities of alkaloids, flavonoids, and phenolic acids. *Pharm Biol.* 2011;49(4):396-402.
- [4] Su Y, Zhao B, Zhou L, et al. Ferroptosis, a novel pharmacological mechanism of anti-cancer drugs. *Cancer Lett.* 2020;483:127-136.
- [5] Ilavenil S, Kim DH, Jeong YI, et al. Trigonelline protects the cardiocyte from hydrogen peroxide induced apoptosis in H9c2 cells. *Asian Pac J Trop Med.* 2015;8(4):263-268.
- [6] Arlt A, Sebens S, Krebs S, et al. Inhibition of the Nrf2 transcription factor by the alkaloid trigonelline renders pancreatic cancer cells more susceptible to apoptosis through decreased proteasomal gene expression and proteasome activity. *Oncogene.* 2013;32(40):4825-4835.
- [7] Zhang F, Yue H, Dong R, et al. Trigonelline hydrochloride attenuates silica-induced pulmonary fibrosis by orchestrating fibroblast to myofibroblast differentiation. *Respir Res.* 2024;25(1):242.

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