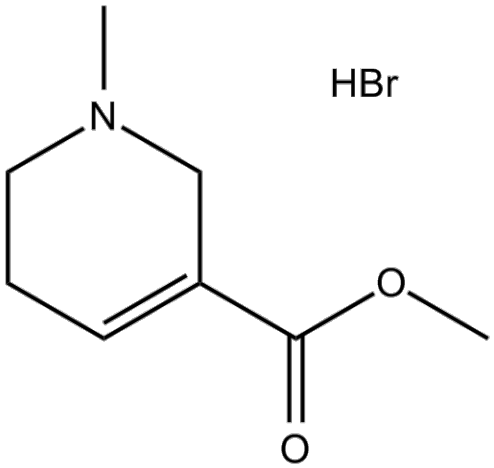
Product Data Sheet

Product Name: Arecoline hydrobromide
Cat. No.: GC10264

Chemical Properties

Cas. No.	300-08-3		
Chemical Name	methyl 1-methyl-3,6-dihydro-2H-pyridine-5-carboxylate;hydrobromide		
SMILES	CN1CCC=C(C1)C(=O)OC.Br		
Formula	C8H14BrNO2	M.Wt	236.11
Solubility	≥ 11.8mg/mL in DMSO	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	HaCaT cells (human spontaneously immortalized normal dermal keratinocyte cell line)

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Preparation Method	HaCaT cells were maintained in DMEM supplemented with 10% heat-inactivated fetal bovine serum at 37°C, 5% CO_2. HaCaT cells were serum-starved for 24h and treated with 0-100μg/mL Arecoline hydrobromide in serum-free or low-serum conditions for 24-72h, followed by MTT assay, Trypan Blue exclusion, 5-bromo-2-deoxyuridine incorporation, flow cytometry for cell cycle and ROS, semiquantitative RT-PCR, Western blot for p38/phospho-p38, and catalase activity assay.
Reaction Conditions	0-100μg/mL; 24-72h
Applications	Arecoline hydrobromide decreased HaCaT cell viability and proliferation by inducing G1/G0 cell cycle arrest without p21/Cip1 upregulation, generating reactive oxygen species (ROS), and causing non-apoptotic cell death at higher concentrations. Arecoline hydrobromide upregulated the mRNA expression of HMOX-1, FTL, G6PD, GCLC, GR, and IL-1α, suppressing catalase activity and activating p38 MAPK phosphorylation.
Animal experiment [2]:	
Animal models	Adult male Wistar rats
Preparation Method	Rats were intraperitoneally injected with Alloxan (75mg/kg) once daily for 10 days to induce type 1 diabetes, then intraperitoneally administered Arecoline hydrobromide at 10mg/kg body weight (divided into two equal half doses of 5mg/kg, injected at 11a.m. and 5p.m.) for 10 days. Serum insulin, blood glucose, liver glycogen, serum testosterone/FSH/LH, coagulating gland fructose, seminal vesicle sialic acid, pancreatic pdx-1 and GLUT-2 protein, and ultrastructure of Leydig cells and ventral prostate epithelium were assessed.

Caution: Product has not been fully validated for medical applications. For research use only.
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Dosage form	5mg/kg; i.p.; twice daily; 10 days
Applications	Arecoline hydrobromide increased serum insulin levels, lowered blood glucose levels, improved intraperitoneal glucose tolerance, increased liver glycogen content, increased serum testosterone/FSH/LH levels, increased coagulating gland fructose and seminal vesicle sialic acid contents, enlarged Leydig cell nucleus and increased SER/DCV/CV numbers, enlarged ventral prostate epithelial nucleus and increased SER abundance, and upregulated pancreatic pdx-1 and GLUT-2 protein expression in alloxan-induced diabetic rats.

References:[1] Thangjam GS, Kondaiah P. Regulation of oxidative-stress responsive genes by arecoline in human keratinocytes. J Periodont Res. 2009;44(6):673-682.[2] Saha I, Das J, Maiti B, et al. A Protective Role of Arecoline Hydrobromide in Experimentally Induced Male Diabetic Rats. Biomed Res Int. 2015;2015:136738.

Background

Arecoline hydrobromide is a brain-penetrant non-selective partial agonist of muscarinic acetylcholine receptors M1-M5 (EC_{50}=7nM, 95nM, 11nM, 410nM, 69nM respectively) and a nicotinic acetylcholine receptor agonist. Arecoline hydrobromide causes smooth muscle contraction and stimulates central cholinergic neurotransmission by activating the cholinergic pathway. Arecoline hydrobromide inhibits the PI3K/AKT pathway, ACAT1 tetramer, and hERG potassium channel. Arecoline hydrobromide is used in studies related to cognitive disorders such as Alzheimer's disease, rheumatoid arthritis, diabetic complications, parasitic infections, and oral cancer[1-4].

In vitro, treatment of HaCaT cells with 0-100μg/mL Arecoline hydrobromide for 24-72 hours decreased cell viability and metabolic activity, inhibited cell proliferation, induced G1/G0 phase cell cycle arrest, generated reactive oxygen species, upregulated HMOX-1, FTL, G6PD, GCLC, GR and IL-1α mRNA expression, and suppressed catalase activity[5]. Treatment of H1299 cells with Arecoline hydrobromide for 1-5 days reduced ACAT1 enzyme activity and Y407 phosphorylation, disrupted ACAT1 tetramer formation, increased pyruvate dehydrogenase complex flux, decreased glycolysis rate and lactate production, elevated oxygen consumption rate and intracellular ATP level,

and inhibited cell proliferation[6]. Treatment of A549 and K562 cells with Arecoline hydrobromide for 48 hours decreased cell viability[7].

In vivo, free drinking of 6-20mg/kg Arecoline hydrobromide by C57B1/6Ncr mice for 2 weeks improved memory retention performance in the T-maze active avoidance task[8]. Feeding of C57BL/6 mice with 0.2% cuprizone diet combined with drinking water containing 2.5-5mg/kg Arecoline hydrobromide for 12 weeks increased the percentage of spontaneous alternation behavior in the Y-maze and elevated the MBP/β-actin ratio in the prefrontal cortex[9]. Intraperitoneal injection of 5mg/kg Arecoline hydrobromide twice daily for 10 days in type 1 diabetic Wistar rat model elevated serum insulin levels, lowered blood glucose, increased liver glycogen content, improved intraperitoneal glucose tolerance, elevated serum testosterone, FSH, and LH levels, and increased coagulating gland fructose and seminal vesicle sialic acid contents[10].

References:
[1] Gao W, He Y, Zhang Y, et al. Comprehensive Insights into Arecoline Hydrobromide: Pharmacology, Toxicity, and Pharmacokinetics. Med Sci Monit. 2024 Nov 11;30:e945582.
[2] Wei X, Zhang J, Niu J,et al. Evaluation of arecoline hydrobromide toxicity after a 14-day repeated oral administration in Wistar rats. PLoS One. 2015 Apr 16;10(4):e0120165.
[3] Gregory GG, McConnell JD. The toxicity and efficiency of arecoline hydrobromide in the Tasmanian hydatid control program. Aust Vet J. 1978 Apr;54(4):193-5.
[4] Chen Q, Jiang Z, Zhang J, et al. Arecoline Hydrobromide Enhances Jejunum Smooth Muscle Contractility via Voltage-Dependent Potassium Channels in W/Wv Mice. Physiol Res. 2021;70(3):437-446.
[5] Thangjam GS, Kondaiah P. Regulation of oxidative-stress responsive genes by arecoline in human keratinocytes. J Periodont Res. 2009;44(6):673-682.
[6] Fan J, Lin R, Xia S, et al. Tetrameric acetyl-CoA acetyltransferase 1 is important for tumor growth. Mol Cell. 2016 Dec 1;64(5):859-874.
[7] Ragab AE, Badawy ET, Aboukhatwa SM, et al. In Vitro Characterization of Inhibitors for Lung A549 and Leukemia K562 Cell Lines from Fungal Transformation of Arecoline Supported by In Silico Docking to M3-mAChR and ADME Prediction. Pharmaceuticals. 2022 Oct;15(10):1171.
[8] Flood JF, Smith GE, Cherkin A. Memory retention test performance in mice: Improvement by chronic oral cholinergic drug treatment. Pharmacol Biochem Behav. 1984;21(1):169-173.
[9] Xu Z, Adilijiang A, Wang W, et al. Arecoline attenuates memory impairment and demyelination in

a cuprizone-induced mouse model of schizophrenia. NeuroReport. 2019 Jan;30(2):134-138.
[10] Saha I, Das J, Maiti B, et al. A Protective Role of Arecoline Hydrobromide in Experimentally Induced Male Diabetic Rats. Biomed Res Int. 2015;2015:136738.