Product Data Sheet

Product Name: U0126-EtOH
Cat. No.: GC12807

Chemical Properties

Cas. No.	1173097-76-1		
Chemical Name	(2Z,3Z)-2,3-bis[amino-(2-aminophenyl)sulfanylmethylidene]butanedinitrile;ethanol		
SMILES	CCO.C1=CC=C(C(=C1)N)SC(=C(C#N)C(=C(N)SC2=CC=CC=C2N)C#N)N		
Formula	$C_{18}H_{16}N_6S_2.C_2H_6O$	M.Wt	426.56
Solubility	50 mg/ml in DMSO (Need ultrasonic)	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.		

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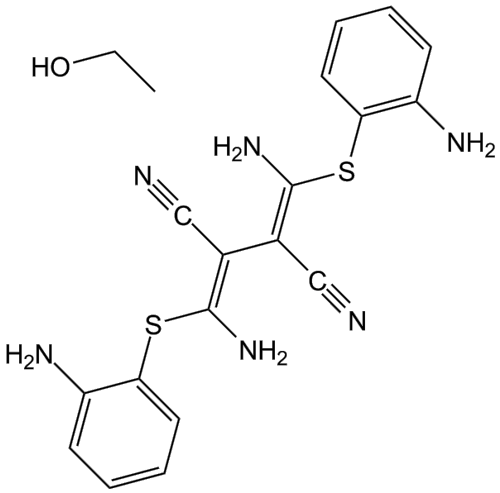
Structure



Protocol

Cell experiment [1]:	
Cell lines	A375 cells

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Preparation Method	A375 cells were cultured in minimal essential medium supplemented with 10% fetal bovine serum, sodium pyruvate, non-essential amino acids, 2mM l-glutamine, 60IU/ml penicillin, and 100IU/ml streptomycin at 37°C with 5% ambient CO_2. The in vitro invasion assay was performed in a 24-well trans-well plate with 8μm pore size filter inserts coated with growth factor reduced Matrigel. Cells (5×10^4) in 500μl minimal essential medium in the absence or presence of different concentrations of U0126-EtOH (0, 1, 5, and 10μM) were plated into Matrigel-coated filter insert. A volume of 800μl of minimal essential medium in the absence or presence of different concentrations of U0126-EtOH (0, 1, 5, and 10μM) was added to the lower compartment of the invasion chamber. The chamber was incubated at 37°C for 8 h in 5% CO_2. After incubation, the cells on the upper side of the insert filter were removed using cotton swabs. Invasion of A375 cells was measured.
Reaction Conditions	0, 1, 5, and 10μM; 8h
Applications	U0126-EtOH treatment reduced invasion of A375 cells in a dose-dependent manner.
Animal experiment [2]:	
Animal models	Male balb/c mice

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Preparation Method	Male balb/c mice (6-week-old) were housed on a 12h light/dark cycle and had free access to food and water at 22°C. Cisplatin was dissolved in normal saline at a concentration of 2mg/ml and mice were given a single intraperitoneal injection of 20mg/kg cisplatin and control animals received same volume of normal saline. One hour before cisplatin administration, either vehicle (0.1% DMSO in normal saline) or U0126-EtOH (10mg/kg) was injected intravenously via tail vein. Mice were sacrificed at 24, 48, and 72 hours after cisplatin administration. Kidneys were collected and processed for histology.
Dosage form	10mg/kg; once; tail vein injection
Applications	U0126-EtOH treatment markedly alleviated acute renal failure induced by cisplatin in mice and reduced renal cell apoptosis.

References:

[1] Ge X, Fu Y M, Meadows G G. U0126, a mitogen-activated protein kinase kinase inhibitor, inhibits the invasion of human A375 melanoma cells[J]. Cancer letters, 2002, 179(2): 133-140.

[2] Jo S K, Cho W Y, Sung S A, et al. MEK inhibitor, U0126, attenuates cisplatin-induced renal injury by decreasing inflammation and apoptosis[J]. Kidney international, 2005, 67(2): 458-466.

Background

U0126-EtOH is a non-ATP competitive and selective inhibitor of MEK1 and MEK2 with IC_{50} values of 72nM and 58nM, respectively[1]. U0126-EtOH inhibits the activity of the ERK signaling pathway, thereby decreasing progesterone production and the expression of steroidogenic enzymes and steroidogenic factor 1 (SF1)[2]. U0126-EtOH has been widely used in parasitological research to inhibit the growth of *Echinococcus granulosus* in mice[3].

In vitro, U0126-EtOH treatment (0.5μM) for 24 hours led to a decrease in the phosphorylation level of

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ERK1/2 and the expression of cyclin D1 in H520 cells[4]. Treatment with 10μM U0126-EtOH in combination with 1μM Purmorphamine for 48 hours inhibited the activity of Rheumatoid arthritis (RA)-fibroblast-like synoviocytes (FLS) cells and altered the distribution of the cell cycle[5]. Treatment with 10μM U0126-EtOH for 8 hours significantly suppressed the invasion of A375 cells and reduced the secretion of uPA and MMP-9[6].

In vivo, U0126-EtOH treatment via a single tail vein injection of 10mg/kg alleviated acute renal failure induced by cisplatin in mice and reduced renal cell apoptosis[7]. Intraperitoneal injection of U0126-EtOH (30mg/kg) at 0 hour and 24 hours after reperfusion improved long-term neurological function in female rats following experimental stroke[8].

References:

[1] Favata M F, Horiuchi K Y, Manos E J, et al. Identification of a novel inhibitor of mitogen-activated protein kinase kinase[J]. Journal of Biological Chemistry, 1998, 273(29): 18623-18632.

[2] Xu P, Bao R, Zhang Y, et al. Prolyl oligopeptidase regulates progesterone secretion via the ERK signaling pathway in murine luteal cells[J]. Molecular reproduction and development, 2019, 86(6): 714-726.

[3] Zhang C, Li J, Aji T, et al. Identification of functional MKK3/6 and MEK1/2 homologs from Echinococcus granulosus and investigation of protoscolecidal activity of mitogen-activated protein kinase signaling pathway inhibitors in vitro and in vivo[J]. Antimicrobial Agents and Chemotherapy, 2019, 63(1): 10.1128/aac. 01043-18.

[4] Fu H, Gao H, Qi X, et al. Aldolase A promotes proliferation and G1/S transition via the EGFR/MAPK pathway in non-small cell lung cancer[J]. Cancer Communications, 2018, 38(1): 18.

[5] Liu F, Feng X X, Zhu S L, et al. Sonic hedgehog signaling pathway mediates proliferation and migration of fibroblast-like synoviocytes in rheumatoid arthritis via MAPK/ERK signaling pathway[J]. Frontiers in immunology, 2018, 9: 2847.

[6] Ge X, Fu Y M, Meadows G G. U0126, a mitogen-activated protein kinase kinase inhibitor, inhibits the invasion of human A375 melanoma cells[J]. Cancer letters, 2002, 179(2): 133-140.

[7] Jo S K, Cho W Y, Sung S A, et al. MEK inhibitor, U0126, attenuates cisplatin-induced renal injury

by decreasing inflammation and apoptosis[J]. Kidney international, 2005, 67(2): 458-466.

[8] Ahnstedt H, Mostajeran M, Blixt F W, et al. U0126 attenuates cerebral vasoconstriction and improves long-term neurologic outcome after stroke in female rats[J]. Journal of Cerebral Blood Flow & Metabolism, 2015, 35(3): 454-460.

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