Small Molecules

U-0126

MEK/ERK pathway inhibitor; Inhibits MEK1 and MEK2

Catalog #	73522	1 mg
	73524	10 mg

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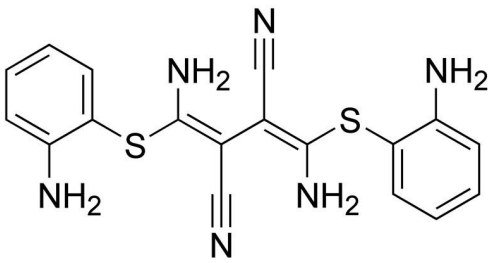
Product Description

U-0126 is a selective, non-ATP competitive inhibitor of mitogen-activated protein kinase kinase (MEK) isoforms MEK1 and MEK2, with IC_{50} values of 72 nM and 58 nM, respectively (Favata et al.; Scherle et al.). It shows little or no inhibition at micromolar levels of other kinases such as extracellular signal-related kinase (ERK), protein kinase C (PKC), c-Jun N-terminal kinases (JNK), other MAP kinase kinases (MKK3, MKK4, MKK6), cyclin-dependent kinases (CDK2, CDK4), ABL, and RAF (Favata et al. 1998). U-0126 also antagonizes AP-1 transcription and selectively inhibits promoters containing AP-1 response elements (Favata et al.).

Molecular Name:	U-0126
Alternative Names:	Not applicable
CAS Number:	109511-58-2
Chemical Formula:	$C_{18}H_{16}N_6S_2$
Molecular Weight:	380.5 g/mol
Purity:	≥ 98%
Chemical Name:	2,3-bis[amino[(2-aminophenyl)thio]methylene]-butanedinitrile
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect from prolonged exposure to light. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 65 mM · Absolute ethanol ≤ 1 mM For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 263 µL of DMSO. Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application. Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

MAINTENANCE AND SELF-RENEWAL
· In combination with FGF2, Activin A (Catalog #78001), and a PKC inhibitor, U-0126 promotes maintenance of human pluripotent stem cells (Kinehara et al.).
· Used alone with MEF-conditioned medium, U-0126 inhibits self-renewal of human pluripotent stem cells, leading to differentiation, without affecting proliferation or survival (Li et al.).
· Inhibits glutamate-induced oxidative stress in mouse hippocampal HT22 cells and rat primary cortical cultures (Ong et al.; Satoh et al.).
· Neuroprotective in a gerbil ischemia model and in primary mouse neurons cultured under hypoxia (Namura et al.).
IMMUNOLOGY
· Inhibits T cell proliferation against certain antigenic stimuli by reducing IL-2 mRNA levels (DeSilva et al.).
DISEASE MODELING
· Activates peroxisome proliferator-activated receptor (PPAR) co-activator 1α (PGC-1α) and prevents neurotoxicity and spatial memory impairment in rats challenged by amyloid beta (Aβ) (Ashabi et al.).

References

Ashabi G et al. (2012) ERK and p38 inhibitors attenuate memory deficits and increase CREB phosphorylation and PGC-1α levels in Aβ-injected rats. Behav Brain Res 232(1): 165–73.
DeSilva DR et al. (1998) Inhibition of mitogen-activated protein kinase kinase blocks T cell proliferation but does not induce or prevent anergy. J Immunol 160(9): 4175–81.
Favata MF et al. (1998) Identification of a novel inhibitor of mitogen-activated protein kinase kinase. J Biol Chem 273(29): 18623–32.
Kinehara M et al. (2013) Protein kinase C regulates human pluripotent stem cell self-renewal. PLoS One 8(1): e54122.
Li J et al. (2007) MEK/ERK signaling contributes to the maintenance of human embryonic stem cell self-renewal. Differentiation 75(4): 299–307.
Namura S et al. (2001) Intravenous administration of MEK inhibitor U0126 affords brain protection against forebrain ischemia and focal cerebral ischemia. Proc Natl Acad Sci USA 98(20): 11569–74.
Ong Q et al. (2015) U0126 protects cells against oxidative stress independent of its function as a MEK inhibitor. ACS Chem Neurosci 6(1): 130–7.
Satoh T et al. (2000) Neuroprotection by MAPK/ERK kinase inhibition with U0126 against oxidative stress in a mouse neuronal cell line and rat primary cultured cortical neurons. Neurosci Lett 288(2): 163–6.
Scherle PA et al. (1998) Inhibition of MAP kinase kinase prevents cytokine and prostaglandin E2 production in lipopolysaccharide-stimulated monocytes. J Immunol 161(10): 5681–6.

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