U0126

#9903 Store at -20°C

5 mg

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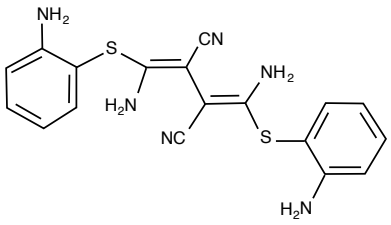
Description: U0126 (1,4-diamino-2,3-dicyano-1,4-bis[2-aminophenylthio] butadiene) has been shown to be a highly selective inhibitor of MEK 1 and MEK 2. When compared with PD98059 #9900, U0126 shows a significantly higher affinity for MEK1. U0126 and PD98059 bind to this enzyme in a mutually exclusive fashion suggesting that they share a common binding site (5). U0126 is able to inhibit both MEK1 and MEK2 while PD98059 inhibits MEK1 more potently than MEK2.

Background: MEK1 and MEK2, also called MAPK or Erk kinases, are dual-specificity protein kinases that function in a mitogen activated protein kinase cascade controlling cell growth and differentiation (1-3). Activation of MEK1 and MEK2 occurs through phosphorylation of two serine residues at positions 217 and 221 (in the activation loop of subdomain VIII) by Raf-like molecules. MEK1/2 is activated by a wide variety of growth factors and cytokines and also by membrane depolarization and calcium influx (1-4). Constitutively active forms of MEK1/2 are sufficient for the transformation of NIH/3T3 cells or the differentiation of PC12 cells (4). MEK activates p44 and p42 MAP kinase by phosphorylating both threonine and tyrosine residues at sites located within the activation loop of kinase subdomain VIII.

Specificity/Sensitivity: U0126 does not inhibit protein kinases including c-Abl, Raf, MEKK, Erk, JNK, MKK3, MKK4/SEK1, MKK6, CDK2 or CDK4.

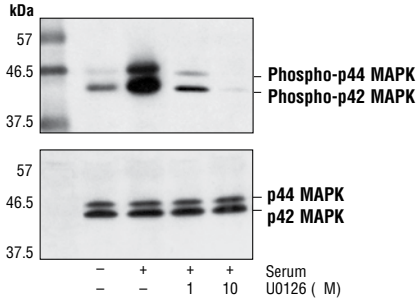
Molecular Formula: 1,4-diamino-2,3-dicyano-1,4-bis[2-aminophenylthio] butadiene ($C_{18}H_{16}N_6S_2$).



Molecular Weight: 380.50 g/mol

Purity: >98%

Directions for Use: U0126 (MEK1/2 Inhibitor) is supplied as a lyophilized white powder. For 10 mM stock, resuspend 5 mg of the inhibitor in 1.31 ml DMSO. Methanol can be substituted for DMSO. Aliquot and freeze at -20°C or below to avoid multiple freeze/thaw cycles which can degrade the inhibitor. For experiments with cultured cells, we recommend pretreating the cells with U0126 at 10 µM for 30 minutes to two hours prior to stimulation. (It may be necessary to use higher concentrations.)



Western blot analysis of extracts from NIH/3T3 cells, using Phospho-p44/42 MAP Kinase (Thr202/Tyr204) Antibody #9101 or control p44/42 MAP Kinase Antibody #9102. NIH/3T3 cells were pretreated with U0126 for 2 hours then treated with 20% serum for 30 minutes.

Background References:

(1) Crews, C.M. et al. (1992) *Science* 258, 478–480.

(2) Alessi, D.R. et al. (1994) *EMBO J.* 13, 1610–1619.

(3) Rosen, L.B. et al. (1994) *Neuron* 12, 1207–1221.

(4) Cowley, S. et al. (1994) *Cell* 77, 841–852.

(5) Favata, M.F. et al. (1998) *J. Biol. Chem.* 273, 18623–18632.

Entrez-Gene ID # 5604, 5605
UniProt ID # Q02750, P36507

Storage: Store lyophilized or in solution at -20°C, desiccated. In lyophilized form, the chemical is stable for 24 months. Once in solution, use within 3 months to prevent loss of potency. Aliquot to avoid multiple freeze/thaw cycles.

Applications Key: **W**—Western **IP**—Immunoprecipitation **IHC**—Immunohistochemistry **ChIP**—Chromatin Immunoprecipitation **IF**—Immunofluorescence **F**—Flow cytometry **E-P**—ELISA-Peptide

Species Cross-Reactivity Key: **H**—human **M**—mouse **R**—rat **Hm**—hamster **Mk**—monkey **Mi**—mink **C**—chicken **Dm**—D. melanogaster **X**—Xenopus **Z**—zebrafish **B**—bovine **Dg**—dog **Pg**—pig **Sc**—S. cerevisiae **All**—all species expected Species enclosed in parentheses are predicted to react based on 100% sequence homology.