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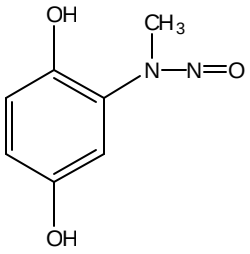
ProductInformation

Dephostatin

Product Number **D8065**

Storage Temperature –20 °C

Cas #: 151606-30-3
Synonyms: 2-(Methylnitrosoamino)-1,4-benzenediol, 2-(N-methyl-N-nitroso)hydroquinone, 1,4-Dihydroxy-N-methyl-N-nitrosoaniline; 3,4-dephostatin



Product Description
Molecular Formula: $C_7 H_8 N_2 O_3$
Molecular Weight: 166.1
Appearance: light yellow powder
Purity: 98% by HPLC

Dephostatin is a selective inhibitor of the protein tyrosine phosphatases (PTPase), including CD45, and SHPTP-1 (SHP-1).

Tyrosine phosphorylation and dephosphorylation are important regulatory components in signal transduction, neoplastic transformation, and the control of cell cycle progression. The activity of enzymes and regulatory proteins is tightly controlled by reversible phosphorylation of serine, threonine or tyrosine residues. PTPases catalyze the hydrolysis of the phosphoester bond of protein-bound phosphotyrosine. PTPases appear to be highly specific for phosphotyrosyl residues and do not structurally resemble either the protein serine/threonine phosphatases or the acid phosphatases and alkaline phosphatases. Mammalian PTPases can be subdivided into two broad categories. Transmembrane receptor PTPases contain linked cytoplasmic catalytic domains, while intracellular PTPases contain two tandem SRC homology 2 (SH2) domains. The transmembrane PTPases are involved in cell-cell or cell-matrix interactions and share properties with adhesion molecules.[1]

Dephostatin was isolated originally from the culture broth of a strain of *Streptomyces* MJ742-NF5. It inhibits PTPase prepared from a human neoplastic T-cell line with an IC_{50} = 7.7 µM. The inhibitory pattern of dephostatin is competitive with the substrate. Dephostatin inhibits CD45, a T-cell receptor-associated transmembrane PTPase found on nucleated hematopoietic cells. CD45, leukocyte common antigen-related PTPase, as well as intracellular PTPases such as SHPTP-1 and SHPTP-2 (SHP-2) have been identified in insulin-sensitive tissues such as skeletal muscle, liver and adipose tissue and may play a roles in the regulation of the insulin receptor and in insulin signaling. [2-4]

Dephostatin has been reported to elevate Ca^{2+} levels by mobilizing calcium from intracellular stores and to induce amylase secretion in pancreatic acinar cells. These effects are reversed by the disulfide reducing agent dithiothreitol and may be due to dephostatin-induced protein oxidation rather than to the inhibition of tyrosine phosphatase activity.[5] The effect of increasing cellular tyrosine phosphorylation through inhibition of endogenous tyrosine phosphatases was examined on voltage-operated calcium channel currents in vascular smooth muscle cells. Intracellular application of the permeant tyrosine phosphatase inhibitors, phenylarsine oxide (100 microM) and dephostatin (50 microM) increased voltage-operated calcium channel currents by 48% and 52%, respectively.[6]

Preparation Instructions
Dephostatin is soluble in DMSO at 22 mg/ml. It is insoluble in water.

Storage/Stability
Store under argon in a desiccator at –20 °C.

References
1. Kaplan, R., et al., Cloning of three human tyrosine phosphatases reveals a multigene family of receptor-linked protein-tyrosine-phosphatases expressed in brain. Proc. Nat. Acad. Sci., **87**, 7000-7004 (1990).

2. Imoto, M., et al., Dephostatin, a novel protein tyrosine phosphatase inhibitor produced by *Streptomyces*. I. Taxonomy, isolation, and characterization. J. Antibiot., **46,** 1342-1346 (1993).
3. Watanabe, T., et al., Total synthesis of dephostatin, a novel protein tyrosine phosphatase inhibitor. J. Chem. Soc. Chem. Commun., **4,** 437-438 (1993).
4. Uesugi, Y., et al., Inhibition of ATRA-induced myeloid differentiation in acute promyelocytic leukemia by a new protein tyrosine phosphatase inhibitor, 3,4-dephostatin. J. Exp. Clin. Cancer Res., **19**, 363-366 (2000).
5. Lajas, A.I., et al., Effect of dephostatin on intracellular free calcium concentration and amylase secretion in isolated rat pancreatic acinar cells. Mol.Cell Biochem., **205**, 163-169 (2000).
6. Wijetunge, S., et al., Effect of inhibition of tyrosine phosphatases on voltage-operated calcium channel currents in rabbit isolated ear artery cells. Br. J Pharmacol., **124**, 307-316 (1998).

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