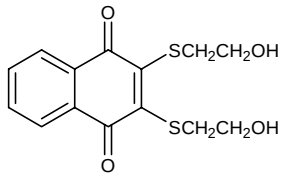
3050 Spruce Street
Saint Louis, Missouri 63103 USA
Telephone 800-325-5832 • (314) 771-5765
Fax (314) 286-7828
email: techserv@sial.com
sigma-aldrich.com

ProductInformation

NSC 95397

Product Number **N 1786**
Storage Temperature –0 °C

Cas #: 93718-83-3
Synonyms: 2,3-bis-[(2-Hydroxyethyl)thio]-1,4-naphthoquinone



Product Description
Molecular Formula: $C_{14}H_{14}O_4S_2$
Molecular Weight: 310.39
Appearance: Orange solid
Purity: 97% by HPLC
m.p.: 116.3-116.9 °C

Many events in cell signaling, transcription, and mitosis are regulated by reversible protein phosphorylation, which is the product of dynamic balance between the enzymatic activity of protein kinases (phosphorylation) and protein phosphatases (dephosphorylation). Dual specificity protein phosphatases uniquely dephosphorylate both phosphoserines/threonines and phosphotyrosines on the same protein substrate. They regulate intracellular signaling through mitogen activated and stress activated kinases, oncogenesis and cell cycle progression through G_1/S and G_2/M checkpoints. The Cdc25 dual phosphatases have been implicated in cancer and Alzheimer's disease.[1,2] Three Cdc25 homologs exist in humans and are referred to as Cdc25A, Cdc25B, and Cdc25C. They are expressed and activated at different times during the cell cycle. Cdc25A is overexpressed in 47% of breast cancer patients. It correlates with higher levels of Cdk2 activity *in vivo* and with poor survival prognosis.[2]

NSC 95397 is a potent and selective irreversible inhibitor of Cdc25 dual specificity phosphatase. Its mechanism of action involves inhibition of the catalytic activity of Cdc25. NSC 95397 inhibits *in vitro* oncogenic, full-length, recombinant human Cdc25B with IC_{50} < 500 nM.[3] *In vitro* inhibition of Cdc25A, -B, and -C displays K_i values of 32, 96, and 40 nM, respectively.[3]

NSC 95397 is 125- to 180-fold more selective for Cdc25A than VH1-group of dual specificity phosphatases or protein tyrosine phosphatase PTP1B, respectively.[3] The compound significantly inhibits *in vitro* growth of human and murine carcinoma cells and blocks G_2/M cell cycle phase transition.[3]

Small molecules that either inhibit the catalytic activity or alter the subcellular distribution of dual specificity protein phosphatases could provide effective tools to study the role of phosphorylation pathways in cell cycle progression and oncogenesis.

Preparation Instructions
NSC 95397 is soluble in DMSO at 16 mg/ml.

Storage/Stability
Store at –0 °C in a freezer.

References
1. Pestell, K. E., et al., Small molecule inhibitors of dual specificity protein phosphatases. Oncogene, **19**, 6607-6612 (2000).
2. Cangi, M. G., et al., Role of Cdc25A phosphatase in human breast cancer. J. Clin. Invest., **106**, 753-761 (2000).
3. Lazo, J.S., et al., Identification of a potent and selective pharmacophore for Cdc25 dual specificity phosphatase inhibitors. Mol. Pharmacol., **61**, 720-728 (2002).

AH 3/03