Small Molecules

Splitomicin

Epigenetic modifier; Inhibitor of Sir2p

Catalog # 73842

5 mg

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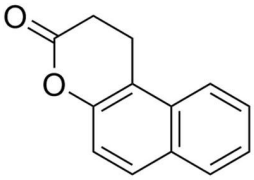
Product Description

Splitomicin is a cell-permeable, selective inhibitor of Sir2p NAD+-dependent histone deacetylase (HDAC) activity. Sir2p negatively regulates gene expression and initiation of DNA replication. Splitomicin induces dose-dependent inhibition of the HDAC activity of Sir2p in vitro (IC_{50} = 60 µM) and in vivo (minimal inhibitory concentration = 0.49 µM) in yeast extract (Bedalov et al.; Hirao et al.). It was shown that the hydrolytically unstable lactone ring of Splitomicin is critically important for its activity (Posakony et al.).

Molecular Name:	Splitomicin
Alternative Names:	1-Naphthalenepropanoic Acid
CAS Number:	5690-03-9
Chemical Formula:	$C_{13}H_{10}O_2$
Molecular Weight:	198.2 g/mol
Purity:	≥ 98%
Chemical Name:	1,2-dihydro-3H-naphtho[2,1-b]pyran-3-one
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect product from prolonged exposure to light. For long-term storage store with a desiccant. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 75 mM · Absolute ethanol ≤ 75 mM For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 505 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

IMMUNOLOGY
· Inhibits platelet aggregation induced by thrombin, collagen, arachidonic acid, and U46619 (Liu et al.).
DISEASE MODELING
· Reactivates FMR1 expression in neurons of Fragile X patients in vitro (Biacsi et al.).
CANCER RESEARCH
· Sensitizes cancer cells to a variety of DNA-damaging agents by abrogating Sir2p downregulation of p53 expression (Botta et al.).

References

Bedalov A et al. (2001) Identification of a small molecule inhibitor of Sir2p. Proc Natl Acad Sci USA 98(26): 15113–8.
Biacsi R et al. (2008) SIRT1 inhibition alleviates gene silencing in Fragile X mental retardation syndrome. PLoS Genet 4(3): e1000017.
Botta G et al. (2012) Current advances in the synthesis and antitumoral activity of SIRT1-2 inhibitors by modulation of p53 and pro-apoptotic proteins. Curr Med Chem 19(34): 5871–84.
Hirao M et al. (2003) Identification of selective inhibitors of NAD+-dependent deacetylases using phenotypic screens in yeast. J Biol Chem 278(52): 52773–82.
Liu F-C et al. (2009) Splitomicin suppresses human platelet aggregation via inhibition of cyclic AMP phosphodiesterase and intracellular Ca++ release. Thromb Res 124(2):199–207.
Posakony J et al. (2004) Inhibitors of Sir2: evaluation of splitomicin analogues. J Med Chem 47(10): 2635–44.

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This product is hazardous. Please refer to the Safety Data Sheet (SDS).