

Product Data Sheet

Product Name: Splitomicin

Cat. No.: GC10555

Chemical Properties

Cas. No. 5690-03-9

Chemical Name 1,2-dihydrobenzo[f]chromen-3-one

SMILES C1CC(=O)OC2=C1C3=CC=CC=C3C=C2

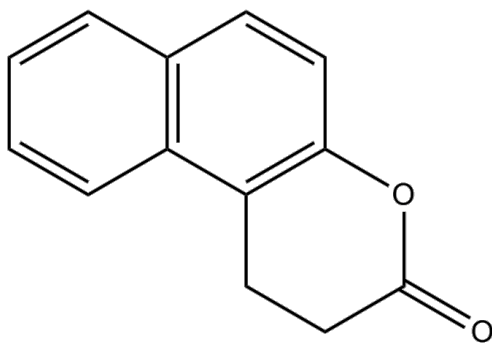
Formula $C_{13}H_{10}O_2$ M.Wt 198.22

Solubility $\geq 9.05\text{mg/mL}$ in DMSO, $\geq 44.2\text{mg/mL}$ in EtOH with ultrasonic Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

Splitomicin is a selective inhibitor of Sir2p with IC_{50} value of $60\text{ }\mu\text{M}$ and also an inhibitor of fMLP-induced free radicals with IC_{50} value of $40.79 \pm 9.85\text{ }\mu\text{M}$ [1, 3].

Inhibition of the HDA of Sir2p was the most likely mechanism by which splitomicin caused its phenotypic changes. The direct target of splitomicin is Sir2p deacetylase activity. In addition, splitomicin specifically inhibited fMLP-induced superoxide anion release.

In vitro, splitomicin inhibited NAD^{+} -dependent histone deacetylase activity of the Sir2 protein with an

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IC50 value of 60 μ M. By using a [3H]-acetylated histone H4 peptide and measuring the NAD⁺-dependent release of free [3H]acetate in the presence of whole yeast cell extract from an hst2 strain overexpressing yeast SIR2, a cell extract was obtained from a SIR2-overexpressing hst2 strain. The result established Sir2p deacetylase activity as a direct target of splitomicin. In addition, neutrophils induced by either fMLP (1 μ M) or PMA (100 nM) were observed using a flow cytometer and the intracellular production of superoxide anions was investigated at different splitomicin concentrations. Splitomicin inhibited fMLP-induced Mac-1 expression and increase cAMP levels in human neutrophils [1, 3].

Splitomicin's naphthoic moiety might be responsible for its inhibitory effects on platelets. By using washed human platelets, the inhibitory effects of splitomicin on platelet aggregation were studied and platelet aggregation and ATP release induced by thrombin (0.1 U/ml), collagen (2 μ g/ml), arachidonic acid (0.5 mM), U46619 (2 μ M) or ADP (10 μ M) was monitored. Splitomicin inhibited platelet aggregation in a concentration dependent manner. Splitomicin increased cAMP and this effect was enhanced when splitomicin (150 μ M) was combined with PGE1 (0.5 μ M). The inhibitory mechanism of splitomicin on platelet aggregation may increase cyclic AMP levels via inhibition of cyclic AMP phosphodiesterase activity and subsequent inhibition of intracellular Ca ion mobilization, TXB2 formation and ATP release [2].

References:

- [1]. Bedalov A, Gatbonton T, Irvine WP, et al. Identification of a small molecule inhibitor of Sir2p. *Proceedings of the National Academy of Sciences of the United States of America*, 2001, 98(26): 15113-15118.
- [2]. Liu FC, Liao CH, Chang YW, et al. Splitomicin suppresses human platelet aggregation via inhibition of cyclic AMP phosphodiesterase and intracellular Ca⁺⁺ release. *Thrombosis Research*, 2009, 124(2): 199-207.
- [3]. Liu FC, Day YJ, Liou JT, et al. Splitomicin inhibits fMLP-induced superoxide anion production in human neutrophils by activate cAMP/PKA signaling inhibition of ERK pathway. *European Journal of Pharmacology*, 2012, 688: 68-75.

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