

Product Name:	21-Hydroxyoligomycin A
Product Number:	H032
CAS Number:	102042-09-1
Molecular Formula:	C ₄₅ H ₇₄ O ₁₂
Molecular Weight:	807.1
Appearance:	White Lyophilisate
Solubility:	Soluble in ethanol, methanol, DMF and DMSO but practically insoluble in water.
Source:	<i>Streptomyces cyaneogriseus</i> ssp. noncyanogenus (LL-F28249)
Storage Conditions:	-20°C
Description:	<p>21-Hydroxyoligomycin A is a rare member of the Oligomycin class, isolated as a co-metabolite of nemadectin, hence it was originally named Nemadectin omega. Only limited literature references are available. In-house testing suggests that 21-Hydroxyoligomycin has a more selective action against mammalian tumor cell lines than Oligomycin A, exhibiting only weak antifungal and nematocidal activity. 21-Hydroxyoligomycin A can Inhibit K-Ras plasma membrane localization and is therefore a putative anti-cancer agent.</p> <p>21-Hydroxyoligomycin A is soluble in ethanol, methanol, DMF and DMSO but practically insoluble in water.</p> <p>Additional Oligomycin products can be found here.</p>
Mechanism of Action:	<p>21-Hydroxyoligomycin A can Inhibit K-Ras plasma membrane localization are therefore putative cancer chemotherapeutic agents. The study of its inhibitory mechanism of action are expected to reveal pathways and molecular targets to control K-Ras (Salim et al, 2016).</p> <p>Single-crystal X-ray analysis established the structure and absolute configuration of 21-hydroxy-oligomycin A (Wagenaar et al, 2017).</p>

Cancer Applications

It is reported to be cytotoxic to human colon cancer SW620 cells (IC₅₀ = 14.4 μM), cytotoxic to human colorectal carcinoma cells (IC₅₀ > 3 μM), to inhibit the ABC transporter efflux pump P-glycoprotein (P-gp).

Ras proteins are membrane-bound GTPases that regulate cell growth, proliferation and differentiation. Mutant forms of Ras are prominent in many human cancers. Oncogenic mutant K-Ras must be localized to the plasma membrane to be functional. 21-Hydroxyoligomycin A prevented K-Ras plasma membrane localization (IC₅₀ = 4.82 nM). The other Oligomycins A-E were also able to inhibit K-Ras plasma membrane localization with (IC₅₀ range of ~ 1.5-14 nM (Wagenaar et al, 2007). I

Inhibitors of K-Ras plasma membrane localization are therefore putative cancer chemotherapeutic agents. The study of K-Ras inhibitory mechanism of action are expected to reveal pathways and molecular targets to control K-Ras. This could inform the development of new probes to better interrogate K-Ras-dependent cancers.

References:

Salim AA et al (2016) Oligomycins as inhibitors of K-Ras plasma membrane localisation. *Org. Biomol. Chem.* 14(2):711-715 PMID 26565618

Thomas DI, Cove JH, Baumberg S, Jones CA and Rudd BA (1991) Plasmid effects on secondary metabolite production by a streptomycete synthesizing an anthelmintic macrolide. *J Gen Microbiol.* 137:2331-2337 PMID 1770350

Wagenaar MM, Williamson RT, Ho DM, and Carter GT (2007) Structure and absolute stereochemistry of 21-Hydroxyoligomycin A.. *J Nat Prod.* 70(3):367-371 PMID 17249728