

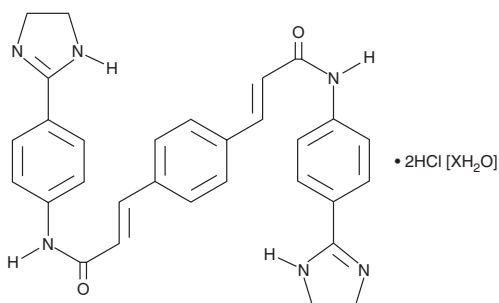
PRODUCT INFORMATION



GW 4869 (hydrochloride hydrate)

Item No. 13127

CAS Registry No.: 6823-69-4
Formal Name: 3,3'-(1,4-phenylene)bis[N-[4-(4,5-dihydro-1H-imidazol-2-yl)phenyl]-dihydrochloride-2-propenamide, hydrate
MF: C₃₀H₂₈N₆O₂ • 2HCl [XH₂O]
FW: 577.5
Purity: ≥90%
UV/Vis.: λ_{max}: 346 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

GW 4869 (hydrochloride hydrate) is supplied as a crystalline solid. A stock solution may be made by dissolving the GW 4869 (hydrochloride hydrate) in the solvent of choice, which should be purged with an inert gas. GW 4869 (hydrochloride hydrate) is soluble in the organic solvent DMSO at a concentration of approximately 0.2 mg/ml.

Description

Neutral sphingomyelinases mediate the release of ceramide from sphingomyelin in cellular membranes and can be activated by certain stresses. Ceramide can act as a signaling molecule in its own right, or it can be further processed to generate sphingosine (and sphingosine-1-phosphate). GW 4869 is an inhibitor of neutral sphingomyelinase (IC₅₀ = 1 μM).¹ It is selective for neutral sphingomyelinase over acid sphingomyelinase at concentrations up to 150 μM as well as *B. cereus* PC-PLC, human lyso-PAF PLC, and bovine PP2A at 10 μM. GW 4869 inhibits TNF-α-induced sphingomyelin hydrolysis by 100% when used at a concentration of 20 μM and TNF-α-induced cell death in MCF-7 cells.^{1,2} It also reduces the inhibitory effects of oxidized 1-palmitoyl-2-arachidonoyl-*sn*-glycero-3-phosphatidylcholine (OxPAPC) and the 5-keto-6-octendioic acid ester of 2-lysophosphatidylethanolamine (KOdiA-PE) on LPS-induction of IL-8 in human aortic endothelial cells.³ *In vivo*, GW 4869 (1 mg/kg) reverses hypoxia-induced pulmonary vasoconstriction in rats.⁴

References

1. Luberto, C., Hassler, D.F., Signorelli, P., *et al.* Inhibition of tumor necrosis factor-induced cell death in MCF7 by a novel inhibitor of neutral sphingomyelinase. *J. Biol. Chem.* **277**(43), 41128-41139 (2002).
2. Marchesini, N., Luberto, C., and Hannun, Y.A. Biochemical properties of mammalian neutral sphingomyelinase 2 and its role in sphingolipid metabolism. *J. Biol. Chem.* **278**(16), 13775-13783 (2003).
3. Walton, K.A., Gugiu, B.G., Thomas, M., *et al.* A role for neutral sphingomyelinase activation in the inhibition of LPS action by phospholipid oxidation products. *J. Lipid. Res.* **47**(9), 1967-1974 (2006).
4. Cogolludo, A., Moreno, L., Frazziano, G., *et al.* Activation of neutral sphingomyelinase is involved in acute hypoxic pulmonary vasoconstriction. *Cardiovascular Res.* **82**(2), 296-302 (2009).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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