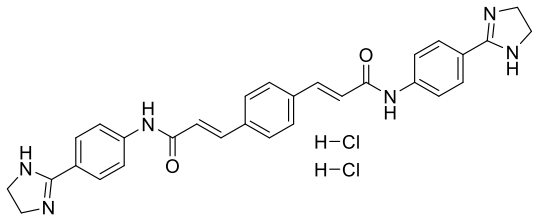
Product data sheet

MedKoo Cat#: 555211 Name: GW-4869 HCl CAS: 6823-69-4 (HCl) Chemical Formula: $C_{30}H_{30}Cl_2N_6O_2$ Molecular Weight: 577.51	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

GW-4869 is a cell-permeable, non-competitive inhibitor of neutral sphingomyelinases (IC50 = 1 μM). It inhibits TNF-α-mediated sphingomyelin hydrolysis (100% inhibition at 20 μM). GW4869 is cytotoxic to high phosphatidylserine-expressing myeloma cells. Blockade of exosome generation with GW4869 dampens the sepsis-induced inflammation and cardiac dysfunction.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	0.89	1.54

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.73 mL	8.66 mL	17.32 mL
5 mM	0.35 mL	1.73 mL	3.46 mL
10 mM	0.17 mL	0.87 mL	1.73 mL
50 mM	0.03 mL	0.17 mL	0.35 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Peng Y, Zhao M, Hu Y, Guo H, Zhang Y, Huang Y, Zhao L, Chai Y, Wang Z. Blockade of exosome generation by GW4869 inhibits the education of M2 macrophages in prostate cancer. BMC Immunol. 2022 Aug 8;23(1):37. doi: 10.1186/s12865-022-00514-3. PMID: 35941539; PMCID: PMC9361607.
2. Huang Y, Li Y, Zhang H, Zhao R, Jing R, Xu Y, He M, Peer J, Kim YC, Luo J, Tong Z, Zheng J. Zika virus propagation and release in human fetal astrocytes can be suppressed by neutral sphingomyelinase-2 inhibitor GW4869. Cell Discov. 2018 Apr 24;4:19. doi: 10.1038/s41421-018-0017-2. PMID: 29707233; PMCID: PMC5913238.

In vivo study

1. Chen J, Zhou R, Liang Y, Fu X, Wang D, Wang C. Blockade of lncRNA-ASLNCS5088-enriched exosome generation in M2 macrophages by GW4869 dampens the effect of M2 macrophages on orchestrating fibroblast activation. FASEB J. 2019 Nov;33(11):12200-12212. doi: 10.1096/fj.201901610. Epub 2019 Aug 20. Erratum in: FASEB J. 2020 Jun 19;: Erratum in: FASEB J. 2020 Aug;34(8):11307-11310. PMID: 31373848; PMCID: PMC6902732.
2. Lallemand T, Rouahi M, Swiader A, Grazide MH, Geoffre N, Alayrac P, Recazens E, Coste A, Salvayre R, Nègre-Salvayre A, Augé N. nSMase2 (Type 2-Neutral Sphingomyelinase) Deficiency or Inhibition by GW4869 Reduces Inflammation and Atherosclerosis in Apoe-/- Mice. Arterioscler Thromb Vasc Biol. 2018 Jul;38(7):1479-1492. doi: 10.1161/ATVBAHA.118.311208. Epub 2018 May 24. PMID: 29794115; PMCID: PMC6039418.

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7. Bioactivity

Biological target:

GW4869 is a noncompetitive neutral sphingomyelinase (N-SMase) inhibitor with an IC_{50} of 1 μM. GW4869 is an inhibitor of exosome biogenesis/release.

In vitro activity

Treatment with GW4869 dramatically reduced the number of ZIKV-positive astrocytes in the infected cultures (Fig. 6f–j). GW4869 treatment also dramatically decreased ZIKV RNA in the supernatants and reduced viral plaque numbers in PFA (Fig. 6k–m). Similarly, treatment with GW4869 significantly decreased EV numbers in ZIKV MR766 strain-infected astrocytes (Fig. 7a and b). GW4869 reduced the levels of Flotillin-2 and tTG (Tissue transglutaminase, another EV marker) in EV lysates (Fig. 7c), suggesting that GW4869 effectively reduces EVs in infected astrocytes. GW4869 treatment markedly decreased ZIKV RNA in infected astrocytes (Fig. 7d) and in supernatants (Fig. 7e). GW4869 treatment also dramatically decreased viral plaque numbers in PFA (Fig. 7f). Together, these data suggest that GW4869 is an effective inhibitor for ZIKV infection in astrocytes.

Reference: Cell Discov. 2018 Apr 24;4:19. https://pubmed.ncbi.nlm.nih.gov/29707233/

In vivo activity

Circulating IL-1β was significantly reduced (47% decrease; Figure XIIA in the online-only Data Supplement) in the plasma of *Apoe*$^{-/-}$/*Smpd3*$^{+/+}$ mice treated by GW4869 in comparison with vehicle-treated mice and in the plasma of *Apoe*$^{-/-}$/*Smpd3*$^{fro/fro}$ mice (57% decrease; Figure XIIB in the online-only Data Supplement). Likewise, the expression of VCAM-1, IL-1β, IL-6, and TNF-α mRNAs was reduced in aortas of mice injected with GW4869 (Figure XIII in the online-only Data Supplement), together with a decreased ceramide content (around 30%; Figure XIV in the online-only Data Supplement). Finally, the number of MoMa-2/IL-1β positive cells was decreased in the aortic sinus of mice treated by GW4869 (Figure 5A and 5B) and in *Apoe*$^{-/-}$/*Smpd3*$^{fro/fro}$ mice (Figure 5C and 5D). Altogether, these data indicated that nSMase2 inhibition decreases vascular inflammation by reducing the recruitment of monocytes to endothelium and macrophage M1 differentiation.

Reference: Arterioscler Thromb Vasc Biol. 2018 Jul;38(7):1479-1492. https://pubmed.ncbi.nlm.nih.gov/29794115/