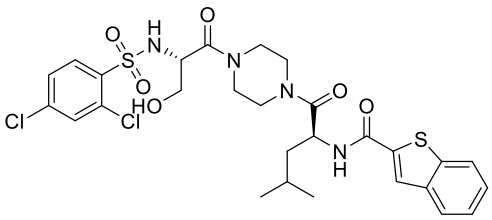
Product data sheet

MedKoo Cat#: 531880 Name: GSK1016790A CAS#: 942206-85-1 Chemical Formula: $C_{28}H_{32}Cl_2N_4O_6S_2$ Exact Mass: 654.114 Molecular Weight: 655.61	
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:
GSK1016790A, also known as GSK101, is a TRPV4 agonist that elicits calcium influx in HEK cells expressing mouse or human TRPV4 (EC50s = 18 and 2.1 nM, respectively).

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	33	50.33

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.53 mL	7.63 mL	15.25 mL
5 mM	0.31 mL	1.53 mL	3.05 mL
10 mM	0.15 mL	0.76 mL	1.53 mL
50 mM	0.03 mL	0.15 mL	0.31 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. Jin M, Wu Z, Chen L, Jaimes J, Collins D, Walters ET, O'Neil RG. Determinants of TRPV4 activity following selective activation by small molecule agonist GSK1016790A. PLoS One. 2011 Feb 14;6(2):e16713. doi: 10.1371/journal.pone.0016713. PMID: 21339821; PMCID: PMC3038856.

2. Thorneloe KS, Sulpizio AC, Lin Z, Figueroa DJ, Clouse AK, McCafferty GP, Chendrimada TP, Lashinger ES, Gordon E, Evans L, Misajet BA, Demarini DJ, Nation JH, Casillas LN, Marquis RW, Votta BJ, Sheardown SA, Xu X, Brooks DP, Laping NJ, Westfall TD. N-((1S)-1-{[4-((2S)-2-{[(2,4-dichlorophenyl)sulfonyl]amino}-3-hydroxypropanoyl)-1-piperazinyl]carbonyl}-3-methylbutyl)-1-benzothiophene-2-carboxamide (GSK1016790A), a novel and potent transient receptor potential vanilloid 4 channel agonist induces urinary bladder contraction and hyperactivity: Part I. J Pharmacol Exp Ther. 2008 Aug;326(2):432-42. doi: 10.1124/jpet.108.139295. Epub 2008 May 22. Erratum in: J Pharmacol Exp Ther. 2011 Jul;338(1):410. PMID: 18499743.

In vivo study

1. Thorneloe KS, Sulpizio AC, Lin Z, Figueroa DJ, Clouse AK, McCafferty GP, Chendrimada TP, Lashinger ES, Gordon E, Evans L, Misajet BA, Demarini DJ, Nation JH, Casillas LN, Marquis RW, Votta BJ, Sheardown SA, Xu X, Brooks DP, Laping NJ, Westfall TD. N-((1S)-1-{[4-((2S)-2-{[(2,4-dichlorophenyl)sulfonyl]amino}-3-hydroxypropanoyl)-1-piperazinyl]carbonyl}-3-methylbutyl)-1-benzothiophene-2-carboxamide (GSK1016790A), a novel and potent transient receptor potential vanilloid 4 channel agonist induces

urinary bladder contraction and hyperactivity: Part I. J Pharmacol Exp Ther. 2008 Aug;326(2):432-42. doi: 10.1124/jpet.108.139295. Epub 2008 May 22. Erratum in: J Pharmacol Exp Ther. 2011 Jul;338(1):410. PMID: 18499743.

2. Pankey EA, Zsombok A, Lasker GF, Kadowitz PJ. Analysis of responses to the TRPV4 agonist GSK1016790A in the pulmonary vascular bed of the intact-chest rat. Am J Physiol Heart Circ Physiol. 2014 Jan 1;306(1):H33-40. doi: 10.1152/ajpheart.00303.2013. Epub 2013 Nov 1. PMID: 24186096; PMCID: PMC3920159.

7. Bioactivity

Biological target:

GSK1016790A is a potent and selective transient receptor potential vanilloid 4 (TRPV4) channel agonist.

In vitro activity

GSK1016790A (GSK101) is a recently discovered specific small molecule agonist of TRPV4. Its effects on physical determinants of TRPV4 activity were evaluated in HeLa cells transiently transfected with TRPV4 (HeLa-TRPV4). GSK101 (10 nM) causes a TRPV4 specific Ca(2+) influx in HeLa-TRPV4 cells, but not in control transfected cells, which can be inhibited by ruthenium red and Ca(2+)-free medium more significantly at the early stage of the activation rather than the late stage, reflecting apparent partial desensitization. Western blot analysis showed that GSK101 activation did not induce an increase in TRPV4 expression at the plasma membrane, but caused an immediate and sustained downregulation of TRPV4 on the plasma membrane in HeLa-TRPV4 cells. Patch clamp analysis also revealed an early partial desensitization of the channel which was Ca(2+)-independent. FRET analysis of TRPV4 subunit assembly demonstrated that the GSK101-induced TRPV4 channel activation/desensitization was not due to alterations in homotetrameric channel formation on the plasma membrane. It is concluded that GSK101 specifically activates TRPV4 channels, leading to a rapid partial desensitization and downregulation of the channel expression on the plasma membrane.

Reference: PLoS One. 2011 Feb 14;6(2):e16713. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/21339821/

In vivo activity

Intravenous injection of GSK1016790A at doses of 2-10 μg/kg produced dose-dependent decreases in systemic arterial pressure, small decreases in pulmonary arterial pressure, and small increases in cardiac output, and responses were not altered by the cyclooxygenase inhibitor meclofenamate or the cytochrome P-450 inhibitor miconazole. Injection of GSK1016790A at a dose of 12 μg/kg iv produced cardiovascular collapse that was reversible in some animals. GSK1016790A produced dose-related decreases in pulmonary and systemic arterial pressure when baseline tone in the pulmonary vascular bed was increased with U-46619. After treatment with the nitric oxide synthase (NOS) inhibitor N-nitro-l-arginine methyl ester, GSK1016790A produced larger decreases in systemic arterial pressure and dose-dependent increases in pulmonary arterial pressure followed by a small decrease. These results demonstrate that GSK1016790A has vasodilator activity in pulmonary and systemic vascular beds and that when NOS is inhibited, GSK1016790A produced pulmonary vasoconstrictor responses that were attenuated by the L-type Ca(2+) channel antagonist isradipine.

Reference: Am J Physiol Heart Circ Physiol. 2014 Jan 1;306(1):H33-40. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24186096/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.