Product data sheet

MedKoo Cat#: 522389 Name: NS6180 CAS#: 353262-04-1 Chemical Formula: $C_{16}H_{12}F_3NOS$ Exact Mass: 323.05917 Molecular Weight: 323.33	
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:

NS6180 is a potent KCa3.1 channel blocker (IC50 values are 9, 14 and 15 nM for rat, human and mouse erythrocyte KCa3.1 channels respectively). NS6180 prevents T-cell activation and inflammation in a rat model of inflammatory bowel disease. NS6180 shows ~ 50% inhibition of KCa1.1, KV1.3, and KV11.1 channels, NS6180 represents a novel class of K(Ca) 3.1 channel inhibitors which inhibited experimental colitis, suggesting K(Ca) 3.1 channels as targets for pharmacological control of intestinal inflammation.**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	20.0	61.9

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	3.09	15.46	30.93
5 mM	0.62	3.09	6.19
10 mM	0.31	1.55	3.09
50 mM	0.06	0.31	0.62

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. Strøbæk D, Brown DT, Jenkins DP, Chen YJ, Coleman N, Ando Y, Chiu P, Jørgensen S, Demnitz J, Wulff H, Christophersen P. NS6180, a new K(Ca) 3.1 channel inhibitor prevents T-cell activation and inflammation in a rat model of inflammatory bowel disease. Br J Pharmacol. 2013 Jan;168(2):432-44. doi: 10.1111/j.1476-5381.2012.02143.x. PMID: 22891655; PMCID: PMC3572569.

In vivo study

1. Strøbæk D, Brown DT, Jenkins DP, Chen YJ, Coleman N, Ando Y, Chiu P, Jørgensen S, Demnitz J, Wulff H, Christophersen P. NS6180, a new K(Ca) 3.1 channel inhibitor prevents T-cell activation and inflammation in a rat model of inflammatory bowel disease. Br J Pharmacol. 2013 Jan;168(2):432-44. doi: 10.1111/j.1476-5381.2012.02143.x. PMID: 22891655; PMCID: PMC3572569.

7. Bioactivity

Biological target:

NS6180 is a novel potent and selective KCa3.1 channel inhibitor (IC50 = 9 nM) that prevents T-cell activation and inflammation (IC50 = 9 nM).

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In vitro activity

The immunisuppressive effects of NS6180 were evaluated in vitro. Similar to TRAM-34, which has previously been used to probe the role of KCa3.1 channels in T- and B-cell activation (Ghanshani et al., 2000; Wulff et al., 2004), NS6180 suppressed both concanavalin (ConA)- and (PMA + ionomycin)-stimulated [3H]-thymidine incorporation of rat splenocytes with IC50s of ∼1 μM and ∼200 nM (Figure 6A). Experiments with WT mouse splenocytes revealed similar inhibitions, whereas splenocytes from KCa3.1–/– mice were insensitive to both compounds (Supplementary Figure S1). NS6180 was equipotent (10–20 nM) with TRAM-34 on both cloned and endogeneous human KCa3.1 channels and showed no species variation for inhibiting KCa3.1-mediated hyperpolarizations from human, rat and mice erythrocytes (Gárdos responses). NS6180 inhibited proliferation stimulated by the lectin ConA, which cross-links T-cell receptors, as well as proliferation driven by the combination of the PKC activator PMA and the calcium ionophore ionomycin, which together stimulate T-cell activation downstream of the T-cell receptor.

Br J Pharmacol. 2013 Jan; 168(2): 432–444. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3572569/

In vivo activity

In order to evaluate NS6180 efficacy in blocking KCa3.1 channels in a disease model, NS6180 was tested in DNBS-induced colitis in rats, a model of human IBD. In keeping with the known expression of KCa3.1 channels in intestinal epithelium (Rufo et al., 1997), immunohistochemical staining for these channels in colon sections from normal rats revealed KCa3.1 channels on the epithelial cells lining the well-aligned parallel crypts (Figure 7, upper panels) and on occasional ED1+ macrophages or CD43+ T cells in the muscularis mucosae and lamina propria (Figure 7, upper panels). In a separate series of experiments, groups of DNBS challenged rats were treated with two doses (3 and 10 mg·kg−1 b.i.d.) of NS6180 for 7 days in direct comparison with the IBD drug sulfasalazine (300 mg·kg−1 q.d.). The disease symptoms were followed, and Figure 8 shows the relative colon (Figure 8A) and body weight development (Figure 8B) of the different groups after 8 days of treatment. Both doses of NS6180 significantly improved weight gain and decreased inflammation induced swelling of the colon as determined by relative colon weight. The positive control sulfasalazine also significantly affected both body weight and colon inflammation (Figure 8). The effects of NS6180 and sulfasalazine did not differ significantly in magnitude.

Br J Pharmacol. 2013 Jan; 168(2): 432–444. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3572569/