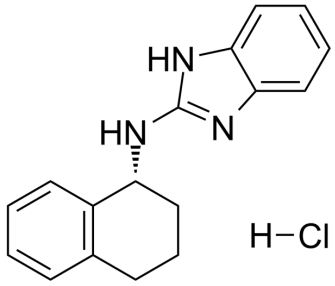
NS8593 hydrochloride

Cat. No.:	HY-110105
CAS No.:	875755-24-1
Molecular Formula:	$C_{17}H_{18}ClN_3$
Molecular Weight:	299.8
Target:	Potassium Channel
Pathway:	Membrane Transporter/Ion Channel
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 83.33 mg/mL (277.95 mM; Need ultrasonic)

H_2O : 1 mg/mL (3.34 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	3.3356 mL	16.6778 mL	33.3556 mL
5 mM	0.6671 mL	3.3356 mL	6.6711 mL
10 mM	0.3336 mL	1.6678 mL	3.3356 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (6.94 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.94 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NS8593 hydrochloride is a potent and selective small conductance Ca^{2+}-activated K^+ channels (SK channels) inhibitor. NS8593 hydrochloride reversibly inhibits SK3-mediated currents with a K_d value of 77 nM. NS8593 hydrochloride inhibits all the SK1-3 subtypes Ca^{2+}-dependently (K_ds of 0.42, 0.60, and 0.73 μM, respectively, at 0.5 μM Ca^{2+}), and does not affect the Ca^{2+}-activated K^+ channels of intermediate and large conductance (hIK and hBK channels, respectively)[1][2].

IC_{50} & Target

Kd: 0.42 μM (SK1), 0.60 μM (SK2) , and 0.73 μM (SK3)[2]

In Vitro

When tested in excised patches, it is found that the inhibition by NS8593 (compound 14) decreased as the intracellular [Ca^{2+}

	] is increased and that NS8593 is equipotent when applied from either the intracellular or the extracellular side of the cell membrane. A HEK293 cell transiently transfected with hSK3 channels is inhibited by 80% upon application of 100 nM apamin and by 75% after application of 300 nM NS8593. In contrast, NS8593 inhibits the mutated channel by 45% at 300 nM. NS8593 thus remains active on the apamin-insensitive SK3 channel, although the K_d value of 0.43 μM is 4-fold higher than found for a wild-type hSK3 channel (K_d of 0.10 μM). As the potency of NS8593 is dependent on the degree of SK3 channel activation, the decreased potency could thus reflect an increased apparent Ca^{2+}-sensitivity of the mutated channels. Similar to the whole-cell experiments, the potency of NS8593 is reduced 3-fold from 0.67 μM to 2.2 μM when tested at a Ca^{2+} concentration of 500 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	NS8593 (compound 14) (3 and 10 mg/kg intravenously) is able to affect firing rate and firing pattern of dopaminergic neurons in vivo in C57Bl/6 mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sørensen US, et al. Synthesis and structure-activity relationship studies of 2-(N-substituted)-aminobenzimidazoles as potent negative gating modulators ofsmall conductance Ca2+-activated K+ channels. J Med Chem. 2008 Dec 11;51(23):7625-34.

[2]. Strøbaek D, et al. Inhibitory gating modulation of small conductance Ca2+-activated K+ channels by the synthetic compound (R)-N-(benzimidazol-2-yl)-1,2,3,4-tetrahydro-1-naphtylamine (NS8593) reduces afterhyperpolarizing current in hippocampal CA1 neurons.

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