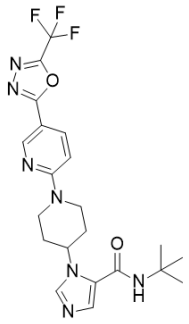
WNK463

Cat. No.:	HY-100626
CAS No.:	2012607-27-9
Molecular Formula:	$C_{21}H_{24}F_3N_7O_2$
Molecular Weight:	463.46
Target:	Ser/Thr Protease
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 30 mg/mL (64.73 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1577 mL	10.7884 mL	21.5768 mL
5 mM	0.4315 mL	2.1577 mL	4.3154 mL
10 mM	0.2158 mL	1.0788 mL	2.1577 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: ≥ 2.5 mg/mL (5.39 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

WNK463 is an orally bioavailable pan-With-No-Lysine (K) (WNK)-kinase inhibitor with IC_{50s} of 5 nM, 1 nM, 6 nM, and 9 nM for WNK1, WNK2, WNK3, and WNK4, respectively[1].

IC_{50} & Target

IC50: 5 nM (WNK1), 1 nM (WNK2), 6 nM (WNK3), and 9 nM (WNK4)[1]

In Vitro

WNK463 (50 nM, 1 μM, 10 μM; 6 days; Human tissue-engineered corneas (hTECs)) treatment reduces phosphorylation of the WNK1 downstream targets SPAK/OSR1 in wounded hTECs.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

Cell Line:	Human tissue-engineered corneas (hTECs)
Concentration:	50 nM, 1 μM, 10 μM
Incubation Time:	6 days
Result:	Reduced phosphorylation of the WNK1 downstream targets SPAK/OSR1 in wounded hTECs.

In Vivo

WNK463 (1-10 mg/kg; oral administration; 4 hours; Spontaneously hypertensive Sprague Dawley rats) treatment produces dose-dependent decreases in blood pressure and simultaneous increases in heart rate in conscious SHRs. WNK463 produces significant and dose-dependent increases in urine output as well as urinary sodium and potassium excretion rates. WNK463 is orally bioavailable in Sprague Dawley rats with a half-life of 2.1 hours[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Spontaneously hypertensive Sprague Dawley rats (34-42 weeks of age) [1]
Dosage:	1 mg/kg, 3 mg/kg, or 10 mg/kg (Pharmacokinetic study)
Administration:	Oral administration; 4 hours
Result:	Decreased in blood pressure and simultaneous increases in heart rate. WNK463 produced significant and dose-dependent increased in urine output as well as urinary sodium and potassium excretion rates.

CUSTOMER VALIDATION

- Cancers. 2020 Mar 2;12(3):575.
- Nat Metab. 2019 Jan;1(1):47-57.

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REFERENCES

[1]. Yamada K et al. Small-molecule WNK inhibition regulates cardiovascular and renal function. Nat Chem Biol. 2016 Nov;12(11):896-898.

[2]. Desjardins P, et al. Contribution of the WNK1 kinase to corneal wound healing using the tissue-engineered human cornea as an in vitro model. J Tissue Eng Regen Med. 2019 Sep;13(9):1595-1608.

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