KHS101 hydrochloride

Cat. No.: HY-10996A

CAS No.: 1784282-12-7

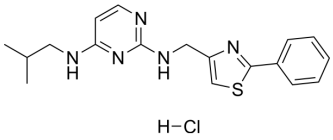
Molecular Formula: $C_{18}H_{22}ClN_5S$

Molecular Weight: 375.92

Target: FGFR

Pathway: Protein Tyrosine Kinase/RTK

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 : 160 mg/mL (425.62 mM; Need ultrasonic)
H_2O : 10 mg/mL (26.60 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6601 mL	13.3007 mL	26.6014 mL
5 mM	0.5320 mL	2.6601 mL	5.3203 mL
10 mM	0.2660 mL	1.3301 mL	2.6601 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: ≥ 2.67 mg/mL (7.10 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.67 mg/mL (7.10 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.67 mg/mL (7.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KHS101 hydrochloride could selectively induce a neuronal differentiation phenotype and interacts with transforming acidic coiled-coil-containing protein 3 (TACC3).

IC_{50} & Target

TACC3[1]

In Vitro

KHS101 increases neuronal differentiation of adherently cultured rat NPCs in a dose-dependent fashion (EC_{50} ~1 μM). KHS101 (1.5–5 μM) induces neuron formation (40-60% TuJ1+ cells) under neurosphere-forming conditions in secondary neurospheres derived from both the hippocampus and the subventricular zone (SVZ) of adult rats.

	Moreover, hippocampal NPCs treated with KHS101 and cultured adherently on microelectrode arrays for 12 d exhibit neuronal morphologies as well as spontaneous spiking activity, hence indicating the presence of functional, maturing neurons[1]. KHS101 markedly attenuates tumor cell growth as compared to the cells treated with the vehicle [dimethyl sulfoxide (DMSO)]. TACC3 is a known target of KHS101 in rodent neural progenitor cells. KHS101 has been shown to cause cellular destabilization of TACC3, hence reducing endogenous TACC3 protein levels over time [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tumor cell proliferation is markedly reduced in KHS101-treated tumors (about twofold). KHS101-treated tumors show signs of elevated cell death (reduced cellularity/increased pyknosis) compared with tumors treated with vehicle control. KHS101 treatment markedly reduces both frontal-to-caudal tumor expansion and corpus callosum invasion of vimentin-positive GBM1 cells. It is also found that the survival of animals carrying GBMX1 tumors (established 2 or 6 weeks before treatment) is markedly increased by the KHS101 treatment regimen for 10 weeks. None of the mice have to be removed from the study because of adverse side effects of the treatment. An additional experiment using a continuous KHS101 treatment regimen until the experimental endpoints also shows a marked increase in the survival of GBMX1-bearing animals. Histological endpoint analysis of KHS101- and vehicle-treated animals confirms a significantly decreased tumor size in KHS101-treated mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Rats[2] Xenograft tumors in rats are allowed to establish for 6 weeks after injection of GBM1 cells (1×10^5 cells) into the forebrain striatum and treated with vehicle or KHS101 for 10 days [6 mg/kg, subcutaneously (sc), twice daily]. To examine whether the observed mitochondrial/redox anomaly is associated with reduced tumor progression, the KHS101 dosing regimen from previous neurogenesis work in rats is adapted using a 10-week tumor treatment strategy (6 mg/kg, sc, twice a day, and biweekly treatment alternating five and three treatment days per week)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Wurdak H, et al. A small molecule accelerates neuronal differentiation in the adult rat. Proc Natl Acad Sci U S A. 2010 Sep 21;107(38):16542-7.

[2]. Polson ES, et al. KHS101 disrupts energy metabolism in human glioblastoma cells and reduces tumor growth in mice. Sci Transl Med. 2018 Aug 15;10(454). pii: eaar2718.

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