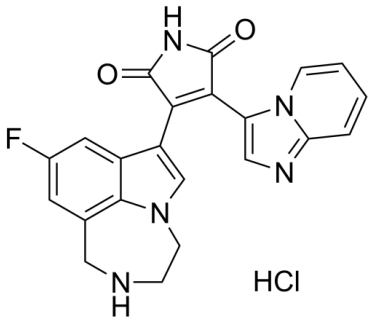
Data Sheet

Product Name:	GSK-3 inhibitor 1
Cat. No.:	CS-2103
CAS No.:	603272-51-1
Molecular Formula:	$C_{22}H_{17}ClFN_5O_2$
Molecular Weight:	437.85
Target:	GSK-3
Pathway:	PI3K/Akt/mTOR; Stem Cell/Wnt
Solubility:	DMSO : 12.5 mg/mL (28.55 mM; ultrasonic and warming and heat to 60°C)



BIOLOGICAL ACTIVITY:

GSK-3 inhibitor 1 (compound core 3) is a **GSK-3** inhibitor that induces stem/progenitor cell self-renewal (e.g. induces stem/progenitor cell proliferation while maintaining the ability to differentiate into tissue cells in the progeny)[1][2]. IC50 & Target:GSK-3[1][2]. ***In Vitro:*** GSK-3 inhibitor 1 can be used to induce, promote or enhance the growth, proliferation or regeneration of inner ear tissues such as inner ear supporting cells or inner ear hair cells[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [1] The human familial Alzheimer's disease (FAD) presenilin-1 AG04160C lymphoblast cell line (Coriell Cell Repository, Camden, NJ) is maintained as a suspension culture in RPMI 1640 (with L-Glutamine) supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin in an atmosphere of 37°C and 5% CO2. The AG04160C FAD lymphoblast cells are seeded in T-25 cm2 flasks at 2.5 to 5.0 X105 cells/ml in a total volume of 10 ml. Following 16-18 hours of growth, cells are treated with compound at concentrations of 0.1 μM, 1.0 μM, and 10 μM, and are incubated for an additional 24 hours. At the completion of the 24-hour incubation, cells are harvested, washed with PBS, and lysed in freshly prepared lysis buffer (10 mM K2HPO4 pH 7.2, 1 mM EDTA, 5 mM EGTA, 10 mM MgCl2, 50 mM β-Glycerophosphate, 1 mM Na3VO4, 2 mM DTT, 1 μM Microcystin, 1 mM PMSF, 10 μg/ml leupeptin, 1 μg/ml pepstatin, 1 μg/ml aprotinin, 1% Triton X-100). After a thirty-minute incubation on ice, cells are centrifuged (14,000 rpm) for 30 minutes at 4°C, and resulting supernatants are used as whole cell lysates. The total protein concentration in whole cell lysate samples is determined using the BCA method (Pierce). Next, 15 μg of sample is loaded on a 10% Bis-Tris NuPage gel and transferred to a pure nitrocellulose membrane followed by β-catenin immunoblot analysis using a β- catenin specific antibody (Transduction Labs). The β-catenin accumulation/stability is then quantified following densitometry analysis of protein bands (Kodak Digital Science). Final results are reported as fold induction over basal β-catenin. The compound of Example 121 was tested in this assay and induced a 9.8-fold induction of β-catenin at 0.1 μM.

References:

[1]. SOLUBILIZED COMPOSITIONS FOR CONTROLLED PROLIFERATION OF STEM CELLS / GENERATING INNER EAR HAIR CELLS USING GSK3 INHIBITORS: III. 20170252449 A1

[2]. Christopher Loose, et al. 1h-pyrrole-2,5-dione compounds and methods of using them to induce self-renewal of stem/progenitor supporting cells. Patent WO2018125746A1.

CAIndexNames:

1H-Pyrrole-2,5-dione, 3-(9-fluoro-1,2,3,4-tetrahydropyrrolo[3,2,1-jk][1,4]benzodiazepin-7-yl)-4-imidazo[1,2-a]pyridin-3-yl-, hydrochloride (1:1)

SMILES:

FC1=CC(CNCC2)=C(N2C=C3C4=C(C5=CN=C6N5C=CC=C6)C(NC4=O)=O)C3=C1.Cl

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