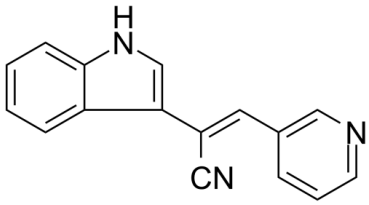
Data Sheet

Product Name:	Paprotrain
Cat. No.:	CS-6861
CAS No.:	57046-73-8
Molecular Formula:	C16H11N3
Molecular Weight:	245.28
Target:	Kinesin
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Solubility:	DMSO : ≥ 100 mg/mL (407.70 mM)



BIOLOGICAL ACTIVITY:

Paprotrain is a cell-permeable inhibitor of the **kinesin MKLP-2**, inhibits the ATPase activity of MKLP-2 with an **IC_{50}** of 1.35 μM and a **K_i** of 3.36 μM and shows a moderate inhibition activity on **DYRK1A** with an **IC_{50}** of 5.5 μM. IC50 & Target: IC50: 1.35 μM (MKLP-2)[4], 5.5 μM (DYRK1A)[1]

Ki: 3.36 μM (MKLP-2)[4] **In Vitro:** Paprotrain has been screened on a panel of CNS kinases. While inactive (IC_{50} >10 μM) on CDK5 and GSK3, it has shown a moderate activity on DYRK1A (IC_{50}=5.5 μM)[1]. Time-lapse microscopy shows that disrupting MKlp2 expression with paprotrain results in polar body extrusion failure. This could be rescued after rescuing oocytes from paprotrain in fresh medium. Cell cycle analysis shows that most oocytes are arrested at metaphase I or telophase I. However, oocyte spindle structure and chromosome alignment are not disrupted after the inhibition of MKlp2 by paprotrain[2]. Paprotrain-treated porcine oocytes suffer failure of nuclear maturation. The number of oocytes arrested at early MI stage increase in a dose-dependent manner after KIF20A activity inhibition, while the percentage of oocytes that reach ATI and MII stages decrease after treatment[3].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Kinase activities for each enzyme are assayed in the presence of 15 μM ATP in a final volume of 30 μL. After 30 min incubation at 30°C, the reaction is stopped by harvesting, using a FilterMate harvester, onto P81 phosphocellulose papers which are washed in 1% phosphoric acid. 20 μL of scintillation fluid are added and the incorporated radioactivity measured in a Packard counter. Blank values are subtracted and activities calculated as pmoles of phosphate incorporated during the 30 min incubation. Controls are performed with appropriate dilutions of DMSO. Kinase activities are expressed in % of maximal activity, i.e. in the absence of inhibitors (Paprotrain). IC50 values are obtained from the dose-response curves[1]. **Cell Assay:** Paprotrain is diluted to50 mM stock solution in dimethyl sulfoxide (DMSO) and stored at −20°C. At the beginning of each culture, the stock solution is diluted with TCM199 to reach final concentrations of 10, 20 and 50 μM[3].[3] COCs or denuded oocytes (DOs) are cultured in the presence/absence of Paprotrain in vitro. The control groups are performed with pure DMSO at the same concentration. COCs are denuded of their cumulus cells by gentle pipetting with 0.1% (w/v) hyaluronidase. Oocytes with clearly extruded polar bodies are judged to be matured oocytes. After cultured for 44 h, the polar body extrusion rate of matured oocytes is observed using a microscope. Furthermore, chromosomal alignments and the cell cycle of oocytes treated with inhibitor are examined using laser scan confocal microscopy[3].

References:

[1]. Labrière C, et al. Further investigation of Paprotrain: Towards the conception of selective and multi-targeted CNS kinase inhibitors. Eur J Med Chem. 2016 Nov 29;124:920-934.

[2]. Liu J, et al. MKlp2 inhibitor paprotrain affects polar body extrusion during mouse oocyte maturation. Reprod Biol Endocrinol. 2013 Dec 21;11:117.

[3]. Zhang Y, et al. KIF20A regulates porcine oocyte maturation and early embryo development.

[4]. Tcherniuk S, et al. Relocation of Aurora B and survivin from centromeres to the central spindle impaired by a kinesin-specific MKLP-2 inhibitor. Angew Chem Int Ed Engl. 2010 Oct 25;49(44):8228-31.

CAIndexNames:

1H-Indole-3-acetonitrile, α-(3-pyridinylmethylene)-, (αZ)-

SMILES:

N#C/C(C1=CNC2=CC=CC=C21)=C\C3=CN=CC=C3

Caution: Product has not been fully validated for medical applications. For research use only.

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