Product Data Sheet

Product Name: JLK 6
Cat. No.: GC13619

Chemical Properties

Cas. No.	62252-26-0		
Chemical Name	7-amino-4-chloro-3-methoxy-1H-isochromen-1-one		
SMILES	COC1=C(Cl)C2=CC=C(N)C=C2C(O1)=O		
Formula	$C_{10}H_8ClNO_3$	M.Wt	225.63
Solubility	<22.56mg/ml in DMSO; <5.64mg/ml in ethanol	Storage	Store at RT
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	JLK 6		

Background

JLK 6, an isocoumarin, is a selective inhibitor of γ-secretase, with an IC50 value between 10 μM-1 mM [1, 2].

The enzyme γ-secretase catalyzes the cleavage of β-Amyloid precursor protein (βAPP) to produce Amyloid β-peptide (Aβ). Aβ is a part of the plaque present in the brain of patients with Alzheimer’s disease. γ-secretase also targets other substrates like Notch. Notch is a transmembrane protein which is involved in important functions during different stages in development, both embryonic and adulthood [1].

HEK293 cells were used. In these cells, wild-type βAPP was overexpressed (962 fmol/mL in 35-mm wells). JLK6 markedly reduced Aβ secreted from these cells. Interestingly, JLK6 potentiated the recovery of two fragments. Immunological characterization indicated that one fragment was labelled with a specific antibody against the Asp1 residue of Aβ. JLK6 also inhibited the Aβ recovery from cells overexpressing Swedish-mutant βAPP to a similar extent [2].

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In the zebrafish embryo, JLK isocoumarin inhibitors did not change the Notch pathway responsible for somitogenesis. Unlike other γ-secretase inhibitors, these agents did not affect E-cadherin processing. JLKs did not inhibit α-secretase, β-site APP cleaving enzymes (BACE) 1 and BACE2, GSK3β kinase and proteasome. JLK inhibitors prevented Aβ production without inducing unwanted cleavages of other proteins [1].

References:

[1]. Petit A, Pasini A, Alves Da Costa C, et al. JLK isocoumarin inhibitors: Selective γ-secretase inhibitors that do not interfere with notch pathway in vitro or in vivo. Journal of neuroscience research, 2003, 74(3): 370-377.
[2]. Petit A, Bihel F, da Costa CA, et al. New protease inhibitors prevent γ-secretase-mediated production of Aβ40/42 without affecting Notch cleavage. Nature cell biology, 2001, 3(5): 507-511.

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