PKC412

Cat. No.: HY-10230
CAS No.: 120685-11-2
Molecular Formula: C₃₅H₃₀N₄O₄
Molecular Weight: 570.64
Target: PKC
Pathway: Epigenetics; TGF-beta/Smad
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: 125 mg/mL (219.05 mM; Need ultrasonic)
H₂O: < 0.1 mg/mL (insoluble)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Mass Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 mM</td>
<td></td>
<td>1.7524 mL</td>
<td>8.7621 mL</td>
<td>17.5242 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.3505 mL</td>
<td>1.7524 mL</td>
<td>3.5048 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.1752 mL</td>
<td>0.8762 mL</td>
<td>1.7524 mL</td>
</tr>
</tbody>
</table>

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: ≥ 2.08 mg/mL (3.65 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.65 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
PKC412 is a multi-targeted protein kinase inhibitor which inhibits PKCα/β/γ, Syk, Flk-1, Akt, PKA, c-Kit, c-Fgr, c-Src, FLT3, PDFRβ and VEGFR1/2 with IC₅₀ ranging from 16-500 nM.

IC₅₀ & Target
IC₅₀: 22 nM (cPKC-α), 30 nM (cPKC-β1), 31 nM (cPKC-β2), 24 nM (cPKC-γ), 330 nM (nPKC-δ), 160 nM (nPKC-η), 1.25 μM (nPKC-ε), 465 μM (aPKC-ζ), 38 nM (PPK), 570 nM (Protein kinase A), 95 nM (c-Syk), 86 nM (KDR), 912 nM (Flt-1), 1.90 μM (Myosin-light chain kinase)⁵

In Vitro
PKC412 shows a broad antiproliferative activity against various tumor and normal cell lines in vitro, and is able to
reverse the Pgp-mediated multidrug resistance of tumor cells in vitro. Exposure of cells to PKC412 results in a dose-dependent increase in the G2/M phase of the cell cycle concomitant with increased polyploidy, apoptosis and enhanced sensitivity to ionizing radiation[1]. Midostaurin with ponatinib induced substantial inhibition of KIT-, Lyn-, and STAT5 activity, but did not suppress Btk in HMC-1 cells and primary neoplastic mast cells[2]. PKC412 inhibits EN fusion tyrosine kinase in hematopoietic Ba/F3 cells. PKC412 significantly inhibits EN phosphorylation in M0-91 and IMS-M2 cells in a dose-dependent manner[3].

In Vivo
PKC412 strongly inhibits retinal neovascularization as well as laser-induced choroidal neovascularization in murine models[1]. PKC412 (25 mg/kg, i.p.) protects mouse livers of the K18 Arg90Cys-overexpressing transgenic mice from Fas-induced apoptosis[4].

PROTOCOL

Cell Assay[3]
Proliferation is determined by trypan blue dye exclusion test. Cells in suspension are seeded in six-well plates at a density of 1×10^5 cells/mL in the presence of different concentrations of PKC412 for 3 days. In control wells, DMSO instead of PKC412 is added. After the treatment, 10 μL of the cell suspension is mixed with 10 μL of 0.4% trypan blue, and alive cells are counted manually using a hemacytometer. Results are calculated as the percentage of the values measured when cells are grown in the absence of the reagent. All experiments are performed in triplicate[3].

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

Animal Administration[4]
K8-deficient, K18-deficient, and human K18 R90C-overexpressing mice with age of 6-8 weeks are used in the assay. Age and sex matched mice are treated with PKC412 (25 mg/kg), daily for 4 d or with an equal volume of DMSO as vehicle (both administered intraperitoneally). On day 5 post-treatment, apoptosis is induced by intraperitoneal injection of Fas ligand (Fas-L) (0.15 μg/g body weight). Mice are fasted overnight before Fas Ab injection, and 18 mice are used per DMSO or PKC412 group for the Fas-treated mice while 6 mice are used per DMSO or PKC412 group for the control non-Fas-treated mice. Mice are sacrificed by CO2 inhalation 6 h after Fas Ab injection. Blood is collected by intracardiac puncture, and livers are harvested for hematoxylin and eosin (HE) staining (after fixation in 10% formalin) or frozen in optimum cutting temperature compound for immunofluorescence staining[4].

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

CUSTOMER VALIDATION

• Cell. 2018 Sep 20;175(1):171-185.e25.
• SLAS Discov. 2018 Jun 1:2472555218777968.

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REFERENCES


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