Product Name: GKT137831
Revision Date: 6/30/2018

Product Data Sheet

Chemical Properties

<table>
<thead>
<tr>
<th>Product Name:</th>
<th>GKT137831</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cas No.:</td>
<td>1218942-37-0</td>
</tr>
<tr>
<td>M.Wt:</td>
<td>394.85</td>
</tr>
<tr>
<td>Formula:</td>
<td>C21H19ClN4O2</td>
</tr>
</tbody>
</table>

Chemical Name: 2-(2-chlorophenyl)-4-(3-(dimethylamino)phenyl)-5-methyl-1H-pyrazolo[4,3-c]pyridine-3,6(2H,5H)-dione

Canonical SMILES: CN(C1=CC=CC2=C(C3=O)C(N(N3C4=CC=CC=C4Cl)=CC(N2C)=O)=C1) C

Solubility: ≥39.5mg/mL in DMSO

Storage: Store at -20°C

General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: Others
Pathways: Others

Description:

Ki: 140 nM and 110 nM

GKT137831 is a specific dual NADPH oxidase Nox1/Nox4 inhibitor, respectively[1].

Both Nox1 and Nox4 expressed in vascular smooth muscle cells (VSMCs) are targeted to discreet
intracellular locations, are differentially regulated in response to growth factors and vascular injury, and are activated by distinct mechanisms.

In vitro: GKT137831 lowers hypoxia-induced H(2)O(2) release, cell proliferation, and TGF-β1 expression and attenuated reductions in PPARγ in HPAECs and HPASMCs. [2] GKT137831 also is a blockade of oxidative stress in response to hyperglycemia in human aortic endothelial cells. [3]

In vivo: In WT and SOD1mut mice, GKT137831 (60 mg/kg i.g.) prevents liver fibrosis and downregulates markers of oxidative stress, inflammation, and fibrosis. [1] In mouse model of chronic hypoxia exposure, GKT137831 (60 mg/kg/d p.o.) attenuates lung PPARγ and TGF-β1 expression of chronic hypoxia–induced right ventricular hypertrophy, vascular remodeling, lung cell proliferation, and hypoxic alterations [2]. GKT137831 (60 mg/kg/d p.o.) also attenuates diabetes mellitus-stimulated atherosclerosis in diabetic apolipoprotein E-deficient mice. [3] Furthermore, GKT137831 prevents the increase of oxidative stress in angII-infused c-hNox4Tg mice, abolishes Akt-mTOR and NF-κB signaling pathway and lowers cardiac remodeling. [4]

Clinical trial: Clinical study has been conducted.

Reference:

Protocol

Cell experiment:

Cell lines
Monolayers of HPAECs and HPASMCs, Pulmonary artery endothelial cells

Preparation method
Soluble in DMSO. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
### Applications

GKT137831 (5 μM, 20 μM) attenuated hypoxia-induced HPAECs and HPASMCs proliferation. GKT137831 (20 μM) attenuated hypoxia-induced H2O2 generation in HPAECs and HPASMCs. During the entire 72-hour hypoxia exposure, GKT137831 administration during the last 24 hours attenuated hypoxia-induced reductions in HPAEC and HPASMCP PARγ expression.

### Animal experiment [3]:

<table>
<thead>
<tr>
<th>Animal models</th>
<th>C57Bl/6 mice exposed to normoxic or hypoxic conditions for 3 weeks, wild-type (WT) and SOD1G37R mutant C57BL/6J mice, Diabetic apolipoprotein E-deficient mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage form</td>
<td>Oral gavage, 30 or 60 mg/kg/d, daily for 10 days</td>
</tr>
<tr>
<td>Applications</td>
<td>GKT137831 (30 or 60 mg/kg/d) attenuated chronic hypoxia-induced right ventricular hypertrophy, pulmonary vascular remodeling, increases in vessel wall thickness, and proliferation. GKT137831 attenuated hypoxia-induced reductions in PARγ and increased in TGF-β1 expression. In WT and SOD1mut mice, GKT137831 (60 mg/kg, intragastric (IG) injection) blocked liver fibrosis and downregulated markers of oxidative stress, inflammation, and fibrosis. In diabetic apolipoprotein E-deficient mice, GKT137831 (60 mg/kg/d, p.o.) attenuated diabetes mellitus-accelerated atherosclerosis.</td>
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<tr>
<td>Other notes</td>
<td>Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.</td>
</tr>
</tbody>
</table>

### Reference:


Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short-term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

ApexBio Technology

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