Product Name: Pirfenidone

Chemical Properties

Product Name: Pirfenidone
Cas No.: 53179-13-8
M.Wt.: 185.22
Formula: C12H11NO
Synonyms: N/A
Chemical Name: 5-methyl-1-phenylpyridin-2-one
 Canonical SMILES: CC1=CN(C(=O)C=C1)C2=CC=CC=C2
Solubility: ≥38.4 mg/mL in DMSO, ≥7.68 mg/mL in H2O with gentle warming, ≥36 mg/mL in EtOH
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: TGF-β / Smad Signaling
Pathways: SMAD
Description:
Pirfenidone, an oral antifibrotic agent, has a broad-spectrum of antifibrotic and anti-inflammatory effects. Pirfenidone has beneficial effects for the treatment of certain fibrotic diseases, and is under clinical trials in patients with idiopathic pulmonary fibrosis.
In vitro: In RAW264.7 cells, Pirfenidone (< 300 μg/mL) suppressed the proinflammatory cytokine tumor necrosis factor-α (TNF-α) through a translational mechanism, which was independent of activation of the mitogen-activated protein kinase (MAPK)2, p38 MAP kinase, and c-Jun.
N-terminal kinase (JNK)[1]. In LN-18, T98G, LNT-229 and LN-308 cell lines, Pirfenidone (< 10 mM) reduced glioma cell density in a concentration-dependent manner. In CCL-64 cells, Pirfenidone (< 5 mM) reduced TGF-β bioactivity by affecting TGF-β2 mRNA expression and processing of pro-TGF-β. Pirfenidone (< 8.3 mM) inhibited the activity of recombinant furin and downregulated the expression of MMP-11 in a dose-dependent manner in LN-308 cells[2]. In cultured myometrial and leiomyoma smooth muscle cells, pirfenidone inhibited serum-stimulated increases in DNA synthesis and cell proliferation in a dose-dependent manner[3].

In vivo: In animals, pirfenidone treatment significantly decreased gene expression of collagens I, III and IV, transforming growth factor β-1, Smad-7, TIMP-1 and PAI-1 [4]. Pirfenidone at a dose of 30 mg/kg/day t.i.d. attenuated the bleomycin-induced pulmonary fibrosis. Pirfenidone (30, 100 mg/kg/day t.i.d) suppressed lung inflammatory edema and pulmonary fibrosis. Pirfenidone suppressed the bleomycin-induced increase in lung interleukin (IL)-1β, IL-6, IL-12\p40 and monocyte chemoattractant protein (MCP)-1 levels and prevented the bleomycin-induced decrease in lung interferon (IFN)-γ levels. Furthermore, pirfenidone suppressed elevation of lung basic-fibroblast growth factor (bFGF), transforming growth factor (TGF)-β1 levels, lung stroma cell derived factor (SDF)-1α and IL-18[5].

Pirfenidone (250 mg/kg) potently inhibited the production of the proinflammatory cytokines, TNF-α, interferon-gamma, and interleukin-6, but enhanced the production of the anti-inflammatory cytokine, interleukin-10 in mice [1]. Pirfenidone (250 mg/kg/day) ameliorated cyclosporine-induced fibrosis by about 50% and improved CsA-induced decrease in creatinine clearance. PFD treatment also decreased the TGF-β1 protein expression by 80% in salt-depleted Sprague-Dawley rats [6]. Pirfenidone (400 mg/kg/day) inhibited heat shock protein 47-positive cells and myofibroblasts, the principal cells responsible for the accumulation and deposition of extracellular matrix seen in pulmonary fibrosis in ICR mice intravenously injected with bleomycin[7].

In rats treated with dimethylnitrosamine (10 mg/kg) for 5 weeks, 0.5% pirfenidone reduced the degree of liver injury. Administration of pirfenidone (0.5%, liquid diet) downregulated the elevated levels of those transcripts by 50-60%, and this was associated with a 70% reduction in collagen deposition[8].

Clinical Trials: Pirfenidone is a promising agent for individuals with overt diabetic nephropathy. In the pirfenidone 1200-mg/d group, the mean eGFR increased (+3.3 ± 8.5 ml/min per 1.73 m2) while the mean eGFR decreased in the placebo group (2.2 ± 4.8 ml/min per 1.73 m2; P= 0.026). In the pirfenidone 2400-mg/d group, the dropout rate was high (11 of 25) and the change in eGFR was not significantly different from placebo (1.9 ± 6.7 ml/min per 1.73 m2)[9].

Pirfenidone has entered three Phase III, randomized, double-blind, placebo-controlled studies in patients with idiopathic pulmonary fibrosis (IPF)[10,11]. In the pirfenidone group, as compared with the placebo group, there was a relative reduction of 47.9% in the proportion of patients who had an absolute decline of 10 percentage points and a relative increase of 132.5% in the proportion of patients with no decline in FVC (P < 0.001). Pirfenidone also reduced the decline in the 6-minute walk distance (P = 0.04) and improved progression-free survival (P < 0.001). The most common adverse events were gastrointestinal and skin-related diseases [11].

Reference:
Protocol

**Cell experiment:**

**Cell lines**

LN-308 and CCL-64 cells

**Preparation method**

The solubility of this compound in DMSO is > 9.3 mg/mL. 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.

**Reacting conditions**

Applications

In LN-308 cells, Pirfenidone (< 10 mM) dose-dependently reduced glioma cell. Pirfenidone (< 8.3 mM) also inhibited the activity of recombinant furin and down-regulated the expression of MMP-11 in a dose-dependent manner. In CCL-64 cells, Pirfenidone (< 5 mM) inhibited TGF-β bioactivity by down-regulating TGF-β2 mRNA expression and affecting pro-TGF-β processing.
## Animal experiment [3]:

<table>
<thead>
<tr>
<th>Animal models</th>
<th>SD rats</th>
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<tbody>
<tr>
<td>Dosage form</td>
<td>250 mg/kg/day; p.o.</td>
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<tr>
<td>Applications</td>
<td>In SD rats receiving a low-salt diet, Pirfenidone at the dose of 250 mg/kg/day alleviated cyclosporine-induced fibrosis by approximately 50% and down-regulated TGF-β1 protein expression by 80%. These results indicated that Pirfenidone could attenuate renal fibrosis as well as decreased matrix deposition.</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>
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### 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. Shortterm 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.