# JANEX-1

**Cat. No.:** HY-15508

**CAS No.:** 202475-60-3

**Molecular Formula:** $C_{16}H_{15}N_3O_3$

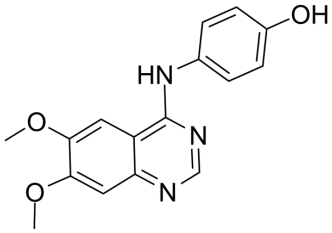
**Molecular Weight:** 297.31

**Target:** JAK

**Pathway:** Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |




## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : ≥ 100 mg/mL (336.35 mM)

* "≥" means soluble, but saturation unknown.

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 3.3635 mL | 16.8175 mL | 33.6349 mL |
| 5 mM | 0.6727 mL | 3.3635 mL | 6.7270 mL |
| 10 mM | 0.3363 mL | 1.6817 mL | 3.3635 mL |

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: ≥ 2.5 mg/mL (8.41 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.41 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.41 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

JANEX-1 (WHI-P131) is a potent and specific JAK3 inhibitor (estimated $K_i$=2.3 μM). JANEX-1 (WHI-P131) shows potent JAK3-inhibitory activity ($IC_{50}$ of 78 μM), does not inhibit JAK1 and JAK2.

**$IC_{50}$ & Target**

JAK3

78 μM ($IC_{50}$)

| | |
|---|---|
| **In Vitro** | JANEX-1 (WHI-P131) shows potent JAK3-inhibitory activity ($IC_{50}$ of 78 μM), does not inhibit JAK1 and JAK2, the ZAP/SYK family tyrosine kinase SYK, the TEC family tyrosine kinase BTK, the SRC family tyrosine kinase LYN, or the receptor family tyrosine kinase insulin receptor kinase, even at concentrations as high as 350 μM. JANEX-1 induces apoptosis in JAK3-expressing human leukemia cell lines NALM-6 and LC1;19 but not in melanoma (M24-MET) or squamous carcinoma (SQ20B) cells. WHI-P131 inhibits the clonogenic growth of JAK3-positive leukemia cell lines DAUDI, RAMOS, LC1;19, NALM-6, MOLT-3, and HL-60 (but not JAK3-negative BT-20 breast cancer, M24-MET melanoma, or SQ20B squamous carcinoma cell lines) in a concentration-dependent fashion. WHI-P131 inhibits clonogenic growth in a concentration-dependent fashion with $EC_{50}$s of 24.4 μM for NALM-6 cells and 18.8 μM for DAUDI cells. At 100 μM, WHI-P131 inhibits the in vitro colony formation by these leukemia cell lines by >99%. In contrast, JANEX-1 does not inhibit the clonogenic growth of JAK3-negative M24-MET melanoma or SQ20B squamous carcinoma cell lines[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | JANEX-1 is administered at doses ranging from 5 to 100 mg/kg. Evaluation of CPK activity revealed a dose-response curve with an effective dose 50 ($ED_{50}$) value of 7.44 mg/kg. Mice receiving JANEX-1 displayed significantly reduced CPK and LDH levels. In addition, the infarct size of JANEX-1-treated mice (30.16±2.79%) is significantly decreased when compared with I/R-operated mice (65.64±3.76%)[2]. JANEX-1 (WHI-P131) is absorbed rapidly, and the time to reach the maximum plasma JANEX-1 concentration ($t_{max}$) is 24.7±1.7 min. JANEX-1 is rapidly eliminated with an elimination half-life of 45.6±5.5 min. Although the predicted maximum plasma JANEX-1 concentration is 10.5 ± 0.8 μM, which is only half of the $C_{max}$ following i.v. administration of the same bolus dose, the i.p. bioavailability is 94.6% and the systemic exposure levels (i.e., AUC) are very similar to those observed after i.v. injection (17.1±2.2 μM•h versus 18.1±1.2 μM•h)[3].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

| | |
|---|---|
| **Cell Assay** [1] | The following cell lines are used in various biological assays: NALM-6 (pre-B-ALL), LC1;19 (pre-B-ALL), DAUDI (B-ALL), RAMOS (B-ALL), MOLT-3 (T-cell ALL), HL60 (acute myelogenous leukemia), BT-20 (breast cancer), M24-MET (melanoma), SQ20B (squamous cell carcinoma), and PC3 (prostate cancer). These cell lines are maintained in culture. Cells are seeded in six-well tissue culture plates at a density of $50\times10^4$ cells/well in a treatment medium containing various concentrations of JANEX-1 (0.1, 0.2, 0.3, 0.4 and 0.5 nM) and incubated for 24-48 h at 37°C in a humidified 5% $CO_2$ atmosphere. Cells are examined for apoptotic changes after treatment with JANEX-1 by the in situ TdT-mediated dUTP end-labeling assay using the ApopTag apoptosis detection kit[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [2][3] | Mice[2]<br>Pathogen-free 8-week-old male $JAK3^{-/-}$ ($129S4\text{-}Jak3^{tm1Ljb}$) and C57BL/6 J mice are used. Mice are treated with JANEX-1 at a dose of 20 mg/kg (intraperitoneally) at 1 h before ischemia.<br>Rats[3]<br>Male Lewis rats are divided into two experimental groups of five and are injected either i.v. via the dorsal vein of the penis or i.p. with a single 3.3 mg/kg bolus dose of JANEX-1. The rats are anesthetized by the methoxyfluran, and blood samples (0.2 mL) are collected from rat tail vein before and at 5, 10, and 30 min and 1, 1.5, 2, 3, 4, and 6 h after i.v. injections or at 5, 10, 15, 30, and 45 min and 1, 1.5, 2, 3, 4, 5, and 7 h after i.p. injections.<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Autophagy. 2018;14(3):450-464.
- Research Square Print. 2023 Feb 28.

- Patent. US20180263995A1.

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## REFERENCES


[1]. Sudbeck EA, et al. Structure-based design of specific inhibitors of Janus kinase 3 as apoptosis-inducing antileukemic agents. Clin Cancer Res. 1999 Jun;5(6):1569-82.

[2]. Oh YB, et al. Inhibition of Janus activated kinase-3 protects against myocardial ischemia and reperfusion injury in mice. Exp Mol Med. 2013 May 17;45:e23

[3]. Uckun FM, et al. In vivo toxicity and pharmacokinetic features of the janus kinase 3 inhibitor WHI-P131 [4-(4'hydroxyphenyl)-amino-6,7- dimethoxyquinazoline. Clin Cancer Res. 1999 Oct;5(10):2954-62.

[4]. Xia F, et al. IL4 (interleukin 4) induces autophagy in B cells leading to exacerbated asthma. Autophagy. 2018;14(3):450-464.





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