Docetaxel

Cat. No.: HY-B0011

CAS No.: 114977-28-5

Molecular Formula: $C_{43}H_{53}NO_{14}$

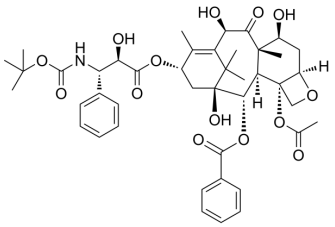
Molecular Weight: 807.88

Target: Microtubule/Tubulin; Apoptosis; Endogenous Metabolite

Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Apoptosis; Metabolic Enzyme/Protease

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (123.78 mM; Need ultrasonic)

Ethanol : 50 mg/mL (61.89 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2378 mL	6.1890 mL	12.3781 mL
	5 mM	0.2476 mL	1.2378 mL	2.4756 mL
	10 mM	0.1238 mL	0.6189 mL	1.2378 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5 mg/mL (6.19 mM); Clear solution
2. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 5 mg/mL (6.19 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution
6. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution
7. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution
8. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution
9. Add each solvent one by one: 10% DMSO >> 90% corn oil

	Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution 10. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution 11. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution 12. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (2.57 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Docetaxel (RP-56976) is a microtubule depolymerization inhibitor, with an IC_{50} of 0.2 μM. Docetaxel attenuates the effects of bcl-2 and bcl-xL gene expression. Docetaxel arrests the cell cycle at G2/M and leads to cell apoptosis. Docetaxel has anti-cancer activity[1][3].
IC_{50} & Target	Microtubule[1]
In Vitro	Docetaxel (RP-56976) and Glufosfamide (GLU) single and combined treatments affect the cells viability in a dose-dependent manner. The IC_{50} of GLU are 70±4 μM and 86.8±8 μM in PC-3 and LNCaP cells; respectively. While, the IC_{50} of Docetaxel alone is found to be 3.08±0.4 nM and 1.46±0.2 nM in PC-3 and LNCaP cells; respectively. The co-treatment of GLU with Docetaxel is found to synergize the cytotoxicity and the IC_{50} values are decreased to be 2.7±0.1 nM and 0.75±0.3 nM in PC-3 and LNCaP cells; respectively[1]. IC_{50} of NCI-H460 to Docetaxel at 24 h is 116 nM and at 72 h is 30 nM. According to data reported in DTP Data Search, the mean IC_{50} of NCI-60 cell panel to Docetaxel is 14-34 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In female mice, the Docetaxel (RP-56976)-induced intestinal apoptosis in the 14-hours after light on (HALO) group is significantly greater than that in the 2-HALO group. Bax expression is significantly elevated by Docetaxel in the 2-HALO group, but not in the 14-HALO group. On the other hand, cleaved Caspase-3 expression is significantly elevated by Docetaxel in the 14-HALO group, but not in the 2-HALO group. The expressions of Wee1 and phosphorylated CKD1 are significantly elevated after dosing of Docetaxel at 14 HALO, but not at 2 HALO. In addition, Docetaxel significantly reduces survivin expression in the 14-HALO group but not in the 2-HALO group. The survivin expression level in the Docetaxel-treated 14-HALO group is significantly smaller than that in the drug-treated 2-HALO group[3]. Piperine (PIP) is administrated via intravenous bolus at 3.5 mg/kg and via oral administration at 35 mg/kg and 3.5 mg/kg, while Docetaxel (DOX) is intravenously administrated at 7 mg/kg to Sprague-Daley rats. The co-administrations of PIP at 35 mg/kg via oral administration and Docetaxel at 7 mg/kg via intravenous bolus administration in Sprague-Dawley rats. The combination use of PIP and Docetaxel results in a synergic increase of both their in vivo exposure[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Single-drug concentration-response curves are assessed. Seeding is done at a density of 2,000 cells/well for PC-3 and LNCaP, in 96-well plates. Cells are treated with each single drug and their combination for 72 h at different drug concentrations. Docetaxel is used at concentrations of 0.1-1,000 nM. GLU is used at concentrations of 0.1-300 μm. Cytotoxicity is assessed at the end of drug exposure using SRB assay. Following 72 h exposure the cells are fixed with 10% trichloroacetic acid (150 μL) for 1 h at 4°C. Then, cells are stained for 10 min at room temperature with 0.4% SRB dissolved in 1% acetic acid. The plates are then air dried for 24 h and the dye is made soluble with 150 μL Tris (10 mM, PH 7.4) for 5 min on a shaker at 1,600 rpm. Absorbance is then measured at 545 nM using microplate reader. Results are expressed as the relative percentage of absorbance compared to control[1].

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Animal Administration [3][4]

Mice[3]

Five-week-old male Balb/c mice are used. Docetaxel (0, 10, 20, 30, 40, 60, and 80 mg/kg per week) is given once a week for 3 weeks for mice. Because more than 30 mg/kg per week of Docetaxel causes body weight loss in mice, 20 mg/kg per week of Docetaxel is judged to be the maximum nontoxic dose. Docetaxel (20 mg/kg per week) is given to mice once a week for 3 weeks at one of the following different points (2, 10, 14, or 22 HALO). Seventy-two hours after the final dosing of the agent, the intestinal mucosa of the small intestine (proximal 8 cm) is removed, fixed in 20 N Mildform solution (containing 8% formaldehyde in a buffered solution), and embedded in paraffin blocks, and sections of 5 μm are put on glass slides. Apoptosis is detected using the terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL) method, using the Apop Tag Peroxidase In Situ Apoptosis Detection Kit.

Rats[4]

Male Sprague-Dawley rats with body weight between 230-250 g and age between 6-7 weeks are used. About 25 SD rats are divided into five groups receiving Docetaxel (7 mg/kg, i.v.), PIP (35 mg/kg, p.o.) and their combined administration (DOX+PIP) as well as PIP (3.5 mg/kg, p.o.) and PIP (3.5 mg/kg, i.v.). A day before the drug administrations, the rats are anesthetized. Right jugular vein is cannulated with a polyethylene tubing (0.5 mm ID, 1 mm) for blood collection.

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

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2022 Sep 12;7(1):317.
- J Hematol Oncol. 2023 May 3;16(1):46.
- Eur Urol. 2020 Nov 2;S0302-2838(20)30778-8.
- ACS Nano. 2021 Apr 27;15(4):7179-7194.
- Acta Pharm Sin B. 2020 June 29.

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REFERENCES

[1]. Attia RT, et al. The chemomodulatory effects of glufosfamide on docetaxel cytotoxicity in prostate cancer cells. PeerJ. 2016 Jun 29;4:e2168.

[2]. Che CL, et al. DNA microarray reveals different pathways responding to NSC 125973 and docetaxel in non-small cell lung cancer cell line. Int J Clin Exp Pathol. 2013 Jul 15;6(8):1538-48.

[3]. Obi-Ioka Y, et al. Involvement of Wee1 in the circadian rhythm dependent intestinal damage induced by docetaxel. J Pharmacol Exp Ther. 2013 Oct;347(1):242-8.

[4]. Li C, et al. Non-linear pharmacokinetics of piperine and its herb-drug interactions with docetaxel in Sprague-Dawley rats. J Pharm Biomed Anal. 2016 Sep 5;128:286-93.

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