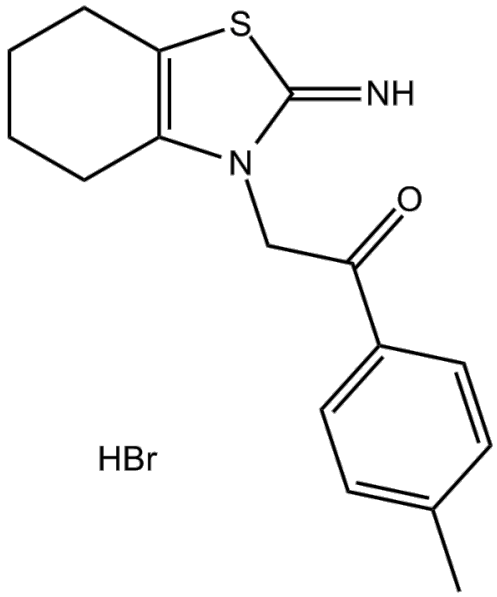
Product Data Sheet

Product Name: Pifithrin-α (PFTα)
Cat. No.: GC10538

Chemical Properties

Cas. No.	63208-82-2		
Chemical Name	2-(2-imino-4,5,6,7-tetrahydro-1,3-benzothiazol-3-yl)-1-(4-methylphenyl)ethanone;hydrobromide		
SMILES	CC1=CC=C(C=C1)C(=O)CN2C3=C(CCCC3)SC2=N.Br		
Formula	$C_{16}H_{18}N_2OS.HBr$	M.Wt	367.3
Solubility	≥ 17.45 mg/mL in DMSO, ≥ 7.12 mg/mL in EtOH with ultrasonic and warming	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.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

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Cell experiment [1]:

Cell lines	HepG2 cells
Preparation Method	Cells seeded in a 96-well plate at a concentration of 10^5 cells/ml for 24 h, were treated with various does TPT, PFTα alone or both (for this group, cells were pretreated with PFTα for 2 h prior to TPT treatment). After 48 h incubation, the cells were pretreated with PFTα for 2 h prior to TPT treatment)
Reaction Conditions	1-100 μM; 2 h
Applications	The *IC_{50} of TPT for HepG2 cells after 10 μμ PFTα pretreated, was lower than the effect of TPT alone. PFTα decreases the p-p53 levels and p-p53 activity.*

Animal experiment [2]:

Animal models	Adult male Sprague-Dawley rats
Preparation Method	Transient Focal Ischemia Model
Dosage form	0.4μg/μl; 20μl; i.c.v + 0.2mg/100gm, i.p; twice a day for three days
Applications	Delayed Pifithrin-α treatment improved locomotor behavior in stroke rats.

Caution: Product has not been fully validated for medical applications. For research use only.
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References:

[1]. Guo J, Tang Q, et,al. Pifithrin-α enhancing anticancer effect of topotecan on p53-expressing cancer cells. Eur J Pharm Sci. 2019 Feb 1;128:61-72. doi: 10.1016/j.ejps.2018.11.024. Epub 2018 Nov 22. PMID: 30472223.
[2]. Luo Y, Kuo CC, et,al. Delayed treatment with a p53 inhibitor enhances recovery in stroke brain. Ann Neurol. 2009 May;65(5):520-30. doi: 10.1002/ana.21592. PMID: 19475672; PMCID: PMC2690614.

Background

Pifithrin-α(PFT-α) is a p53 inhibitor[1]. Pifithrin-α widely used in neuroscience to block neuronal apoptotic cell death[2]. Pifithrin-α is also a potent stimulant of aryl hydrocarbon receptor (AhR) [3].

Pifithrin-α (10 μM;48h) reduces meth-induced degeneration of dopaminergic neurons [4]. Treatment with Pifithrin-α(1 μM; 12-24 h) prevents ROS formation in hMp84-overexpressing A375 cells[5]. The IC_{50} of TPT for HepG2 cells after 10 μμ PFTα pretreated(1-100 μM; 2 h), was 4.8 to 14.4 folds lower than the effect of TPT alone. PFTα decreases the p-p53 levels and p-p53 activity, not affects p53 expression in p53 positive tumor cells[6].

Pifithrin-α (2 mg/kg; i.v) reduced the number of apoptotic cells in the ischemic brain by inhibiting the binding of p53 to its DNA sites as it reduced the expression of the p53-related gene p21WAF[7].Delayed Pifithrin-α (0.4μg/μl; 20μl; i.c.v + 0.2mg/100gm, i.p; twice a day for three days) treatment improved locomotor behavior in stroke rats[8]. Pifithrin-α reduced dopaminergic neurodegeneration in animal models of Parkinson s disease(10 μg)[9], prevented cell death of dopaminergic transplants in 6-OHDA-lesioned rats(2 mg/kg/day; i.p ; 5 days)[10], improved the survival of neuroprogenitor cells in subventricular zone of stroke rats, and reduced traumatic brain injury[11].

References:
[1]. Komarov PG, Komarova EA, et,al. A chemical inhibitor of p53 that protects mice from the side effects of cancer therapy. Science 285:1733-1737

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[2]. Zhu X, Yu QS, et,al. Novel p53 inactivators with neuroprotective action: syntheses and pharmacological evaluation of 2-imino-2,3,4,5,6,7-hexahydrobenzothiazole and 2-imino-2,3,4,5,6,7-hexahydrobenzoxazole derivatives. J Med Chem 45:5090-5097
[3]. Hoagland MS, Hoagland EM, et,al. The p53 inhibitor pifithrin-alpha is a potent agonist of the aryl hydrocarbon receptor. J Pharmacol Exp Ther. 2005 Aug;314(2):603-10. doi: 10.1124/jpet.105.084186. Epub 2005 Apr 20. PMID: 15843497.
[4]. Chen YH, Bae E, et,al. Pifithrin-Alpha Reduces Methamphetamine Neurotoxicity in Cultured Dopaminergic Neurons. Neurotox Res. 2019 Aug;36(2):347-356. doi: 10.1007/s12640-019-00050-w. Epub 2019 May 8. PMID: 31069753.
[5]. Moretti D, Del Bello B, et,al. Calpain-3 impairs cell proliferation and stimulates oxidative stress-mediated cell death in melanoma cells. PLoS One. 2015 Feb 6;10(2):e0117258. doi: 10.1371/journal.pone.0117258. PMID: 25658320; PMCID: PMC4319969.
[6]. Guo J, Tang Q, et,al. Pifithrin-α enhancing anticancer effect of topotecan on p53-expressing cancer cells. Eur J Pharm Sci. 2019 Feb 1;128:61-72. doi: 10.1016/j.ejps.2018.11.024. Epub 2018 Nov 22. PMID: 30472223.
[7].Leker RR, Aharonowiz M, et,al. The role of p53-induced apoptosis in cerebral ischemia: effects of the p53 inhibitor pifithrin alpha. Exp Neurol. 2004 Jun;187(2):478-86. doi: 10.1016/j.expneurol.2004.01.030. PMID: 15144874.
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[9]. Liang ZQ, Li YL, et,al. NF-kappaB contributes to 6-hydroxydopamine-induced apoptosis of nigral dopaminergic neurons through p53. Brain Res 1145:190-203
[10]. Chou J, Greig NH, et,al. Enhanced survival of dopaminergic neuronal transplants in hemi-Parkinsonian rats by the p53 inactivator PFT-α. Cell Transplant 20:1351-1359
[11]. Huang YN, Yang LY, et,al. Neuroprotective effects of pifithrin-α against traumatic brain injury in the striatum through suppression of neuroinflammation, oxidative stress, autophagy, and apoptosis. Sci Rep. 2018 Feb 5;8(1):2368. doi: 10.1038/s41598-018-19654-x. PMID: 29402897; PMCID: PMC5799311.

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