

Product Data Sheet

Product Name: PS-1145

Cat. No.: GC17603

Chemical Properties

Cas. No. 431898-65-6

Chemical Name N-(6-chloro-9H-pyrido[3,4-b]indol-8-yl)nicotinamide

SMILES C1C=CC(C2=CC=NC=C2N3)=C3C(NC(C4=CN=CC=C4)=O)=C1

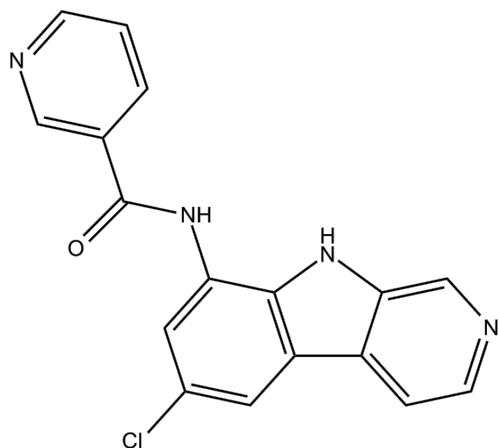
Formula $C_{17}H_{11}ClN_4O$ M.Wt 322.75

Solubility $\geq 32.3\text{mg/mL}$ 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.

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

Structure



Protocol

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

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Cell experiment: The inhibitory effect of PS-1145 on MM growth is assessed by measuring MTT dye absorbance of the cells. MM.1S cells are cultured for 48 h with 0.2 and 1 ng/mL TNF α , in the absence or presence of 2.5 μ M, 5 μ M, and 10 μ M PS-1145. Cell viability is assessed by MTT assay. Cells from 48 h cultures are pulsed with 10 μ L of 5 mg/mL MTT to each well for the last 4 h of 48-h cultures, followed by 100 μ L of isopropanol containing 0.04N HCl. Absorbance is measured at 570 nm using a spectrophotometer[1].

Animal experiment: Mice[2]C57BL/6 (B6), B10.BR, and B6.SJL mice are used. Mice receive regular mouse chow and acidified tap water ad libitum. Bortezomib is administered intravenously to animals at a dose of 1 mg/kg, whereas PS-1145 is given intraperitoneally at a dose of 50 mg/kg. The first dose of each agent is administered before conditioning with total body irradiation (TBI). Rats[3]Weight-matched male Wistar rats (320-350 g) are used. Four groups of rats (n=6/group) consume the HFD for a 9-day study period. Animals in each group receive two consecutive icv injections three times/wk. Immediately prior to icv injection of IL-4 (100 ng) or vehicle, all animals receive a pretreatment icv injection of either the IKK β inhibitor PS1145 (10 μ g) or its vehicle (saline). Food intake and body weight are measured daily. Body composition analysis is conducted as above on days 0 and 8. On day 9, animals are euthanized and samples collected.

References:

- [1]. Hideshima T, et al. NF-kappa B as a therapeutic target in multiple myeloma. J Biol Chem. 2002 May 10;277(19):16639-47.
- [2]. Vodanovic-Jankovic S, et al. NF-kappaB as a target for the prevention of graft-versus-host disease: comparative efficacy of bortezomib and PS-1145. Blood. 2006 Jan 15;107(2):827-34.
- [3]. Oh-I S, et al. Central administration of interleukin-4 exacerbates hypothalamic inflammation and weight gain during high-fat feeding. Am J Physiol Endocrinol Metab. 2010 Jul;299(1):E47-53.

Background

1050-00-00

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IC50: 88 nM

PS-1145 is an I κ B kinase (IKK) inhibitor.

The I κ B kinase is an enzyme complex involved in propagating the cellular response to inflammation. This enzyme complex is reported to be part of the upstream NF- κ B signal transduction cascade.

In vitro: Previous study found that PS-1145 could block TNF α -induced NF- κ B activation in a dose- and time-dependent manner in MM cells, which up-regulated I κ B α protein, enhanced blockade of NF- κ B activation. In addition, PS-1145 blocked the protective effect of IL-6 against Dex-induced apoptosis and TNF α -induced ICAM-1 expression was also inhibited by PS-1145. Moreover, PS-1145 inhibited both IL-6 secretion from BMSCs triggered by MM cell adhesion and proliferation of MM cells adherent to BMSCs. However, PS-1145 could only partially inhibit MM cell proliferation. Importantly, it was found that TNF α induced MM cell toxicity in the presence of PS-1145 [1]

In vivo: Animal study showed that the intravenous application of PS-1145 could promote direct apoptosis in DMBA-induced skin tumor in male Wistar rats via blocking NF- κ B and VEGF activities [2].

Clinical trial: Up to now, PS-1145 is still in the preclinical development stage.

References:

- [1] Hideshima T, Chauhan D, Richardson P, Mitsiades C, Mitsiades N, Hayashi T, Munshi N, Dang L, Castro A, Palombella V, Adams J, Anderson KC. NF- κ B as a therapeutic target in multiple myeloma. J Biol Chem. 2002 May 10; 277(19):16639-47.
- [2] Rajmani RS, Gandham RK, Gupta SK, et al. Administration of I κ B-kinase inhibitor PS1145 enhances apoptosis in DMBA-induced tumor in male Wistar rats. Cell Biol Int. 2015 Nov; 39(11):1317-28.

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