

Product Data Sheet

Product Name: HBX 41108

Cat. No.: GC12622

Chemical Properties

Cas. No. 924296-39-9

Chemical Name 7-chloro-9-oxo-9H-indeno[1,2-b]pyrazine-2,3-dicarbonitrile

SMILES C1C=CC=C(C2=NC(C#N)=C(C#N)N=C2C3=O)C3=C1

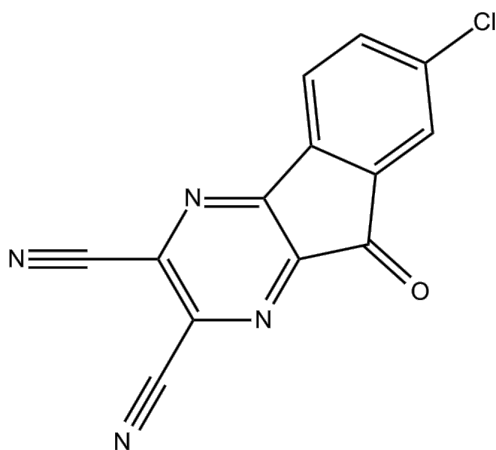
Formula $C_{13}H_3ClN_4O$ M.Wt 266.64

Solubility 33mg/mL in DMSO; 25mg/mL in DMF; 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

Cell experiment [1]:

Cell lines HCT116

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method The exponentially growing HCT116 cells were co-incubated with HBX 41108 for 24h, and then detect its effect on intracellular p53 levels.

Reaction Conditions 1, 3 and 10 μ M; 24h

Applications Western blot analysis revealed that the levels of p53 and its target gene products, such as the cyclin-dependent kinase inhibitor p21^{cip1/waf}, increased in a dose-dependent manner with changes in HBX 41108 concentration.

Animal experiment [2]:

Animal models SD rats; male; 4-6 weeks; 180-200g

Preparation Method Rats were randomized into three groups: in the control group, rats received saline; in the diabetic group, rats were intraperitoneal administrated with 60mg/kg STZ citrate buffer to induce diabetes (STZ group); in diabetes+HBX 41108 group, rats received 60mg/kg STZ citrate buffer and 100mg/kg HBX 41108 (HBX 41108 group). Intraperitoneal injected once a day for 14 consecutive days. Make skin wounds in the middle of the rats' back with scissors. Blood and wounds were detected on day 0, 7 and 14. Wound tissue was collected on days 0, 7, and 14 for HE staining. Western blot analysis the expression of USP7, p53, and p21 in wound tissue.

Dosage form 100mg/kg/d; 14d; i.p.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Applications

STZ group had higher blood glucose levels than control group on day 0, 7 and 14 post injury. HBX 41108 group decreased blood glucose levels on 14 post injury. STZ significantly reduced the wound healing rate, whereas the application of HBX 41108 could rescue the STZ-mediated effects. HE showed that newly formed in wounds treated with HBX 41108 on day 7 post-injury. Meanwhile, on day 7 and day 14, the expressions of USP7, p53, and p21 were found to be increased by STZ and decreased by the application of HBX 41108.

References:

- [1]. Colland F, Formstecher E, Jacq X, et al. Small-molecule inhibitor of USP7/HAUSP ubiquitin protease stabilizes and activates p53 in cells. *Mol Cancer Ther.* 2009;8(8):2286-2295.
- [2]. Li X, Wang T, Tao Y, Wang X, Li L, Liu J. Inhibition of USP7 suppresses advanced glycation end-induced cell cycle arrest and senescence of human umbilical vein endothelial cells through ubiquitination of p53. *Acta Biochim Biophys Sin (Shanghai).* 2022;54(3):311-320.

Background

HBX 41108 is a potent inhibitor of USP7 with IC₅₀ value of 424nM [1]. HBX 41108 is shown to affect USP7-mediated p53 deubiquitinating in vitro and in cells [1].

In vitro, HBX 41108 inhibited HCT116 proliferation in a dose-dependent manner with an IC₅₀ value of 1μM. HBX 41108 induced the apoptosis of HCT116 in a dose-dependent manner within the concentration range of 0-16μM. Treatment with 1-10μM HBX 41108 for 24 hours resulted in a dose-dependent increase in the levels of p53 and its target gene products in HCT116. 10-50μM HBX 41108 for 24 hours increased the multi-ubiquitination level of p53 in 293T cells overexpressing USP7 [1]. 5μM HBX 41108 reduced cell cycle arrest and cell senescence in HUVECs treated with AGEs [2]. 20μM HBX 41108 for 2 hours abolished the increase in PPARγ stability induced by HAUSP in COS7 cells [3]. 10μM and 25μM HBX 41108 increased the hTPH2 promoter activity in a dose-dependent manner in RN46A cells [4].

In vivo, HBX 41108 (100mg/kg) decreased blood glucose levels and improved wound healing rate in diabetic rats, via intraperitoneal injection over 14 days [2].

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

References:

- [1]. Colland F, Formstecher E, Jacq X, et al. Small-molecule inhibitor of USP7/HAUSP ubiquitin protease stabilizes and activates p53 in cells. *Mol Cancer Ther.* 2009;8(8):2286-2295.
- [2]. Li X, Wang T, Tao Y, Wang X, Li L, Liu J. Inhibition of USP7 suppresses advanced glycation end-induced cell cycle arrest and senescence of human umbilical vein endothelial cells through ubiquitination of p53. *Acta Biochim Biophys Sin (Shanghai).* 2022;54(3):311-320.
- [3]. Lee KW, Cho JG, Kim CM, et al. Herpesvirus-associated ubiquitin-specific protease (HAUSP) modulates peroxisome proliferator-activated receptor γ (PPAR γ) stability through its deubiquitinating activity. *J Biol Chem.* 2013;288(46):32886-32896.
- [4]. Nawa Y, Kaneko H, Oda M, et al. Functional characterization of the neuron-restrictive silencer element in the human tryptophan hydroxylase 2 gene expression. *J Neurochem.* 2017;142(6):827-840.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA