Product Data Sheet

Product Name: GNF-PF-3777 (8-Nitrotryptanthrin)
Cat. No.: GC33671

Chemical Properties

Cas. No.	77603-42-0		
SMILES	O=C1N2C(C(C3=C2C=CC([N+]([O-])=O)=C3)=O)=NC4=CC=CC=C41		
Formula	$C_{15}H_7N_3O_4$	M.Wt	293.23
Solubility	DMSO : 6.4 mg/mL (21.83 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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:

To study the cellular hIDO2 inhibition of candidate compounds, recombinant plasmid pcDNA3.1(+)-hIDO2 is constructed and transfected into human glioblastoma U87 MG cells which had no IDO1 expression (confirmed by RT-PCR and western blot) therefore eliminated the interference of IDO1. U87 MG cells are cultivated in DMEM containing 50 U/mL penicillin, 50 mg/mL streptomycin, 4500 mg/L glucose, and 10% inactivated FBS at 37°C with 5% CO2 and 95% humidity. When a cell density of 80% confluent monolayer is reached, U87 MG cells are transfected with pcDNA3.1(+)-hIDO2 using the transfection reagent Lipofectamine 2000 according to the manufacturer's instructions. An empty pcDNA3.1(+) expression vector is served as control. After 18 h of incubation, the transfected cells are seeded in 96-well culture plates at a density of 2.5×104 cells/well in a final volume of 200 µL supplemented with 200 µM L-Trp. A serial dilution of the tested compounds is added to the culture medium after an additional 6 h of incubation. The reaction is terminated by addition of 30% (w/v) trichloroacetic acid (10 µL for 140 µL of the reaction mixture) 24 h later. The plates are incubated at 65°C in water bath for 15 min to facilitate the transformation of N-formylkynurenine to L-kynurenine, followed by centrifugation at 13,000× g for 10 min to remove the sediments. 100 µL of the supernatant are then transferred to another 96-well plate and mixed with a same volume of 2% (w/v) 4-dimethylaminobenzaldehyde in acetic acid. The percentages of inhibition of tryptophan degradation or kynurenine production by the compounds are calculated by measuring the absorption at 492 nm using a microplate reader. Cellular IC50s are determined via non-linear regression analysis using GraphPad Prism 5.0[1].

References:

[1]. Li J, et al. Establishment of a human indoleamine 2, 3-

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dioxygenase 2 (hIDO2) bioassay system and discovery of tryptanthrin derivatives as potent hIDO2 inhibitors. Eur J Med Chem. 2016 Nov 10;123:171-9.
[2]. Scovill J, et al. Antitrypanosomal activities of tryptanthrins. Antimicrob Agents Chemother. 2002 Mar;46(3):882-3.
[3]. Hwang JM, et al. Design, synthesis, and structure-activity relationship studies of tryptanthrins as antitubercular agents. J Nat Prod. 2013 Mar 22;76(3):354-67.

Background

8-Nitrotryptanthrin is a derivative of tryptanthrin with diverse biological

activities.[1,2,3,4,5] It inhibits human recombinant indoleamine 2,3-dioxygenase 1 (IDO1; IC_{50} = 0.103 µM) and its enzyme activity in HEK293 cells expressing human IDO1 (IC_{50} = 0.18 µM).[1] 8-Nitrotryptanthrin inhibits the growth of U251 glioblastoma, H522 lung, M14 melanoma, DU145 prostate, and A498 renal cancer cells (GI_{50}s = 4.5, 4.8, 15, 8, and 2 µM, respectively).[2] It is active against *M. tuberculosis*, methicillin resistant *S. aureus* (MRSA), and *M. furfur* (MICs = 0.032, 0.5, and 5 µg/ml, respectively).[3,4] 8-Nitrotyrptanthrin is also active against *T. brucei* (EC_{50} = 0.24 µg/ml).[5]

1.Yang, S., Li, X., Hu, F., et al.Discovery of tryptanthrin derivatives as potent inhibitors of indoleamine 2,3-dioxygenase with therapeutic activity in Lewis lung cancer (LLC) tumor-bearing miceJ. Med. Chem.56(21)8321-8331(2013) 2.Sharma, V.M., Prasanna, P., Seshu, K.V., et al.Novel indolo[2,1-b]quinazoline analogues as cytostatic agents: Synthesis, biological evaluation and structure-activity relationshipBioorg. Med. Chem. Lett.12(17)2303-2307(2002) 3.Hwang, J.-M., Oh, T., Kaneko, T., et al.Design, synthesis, and structure-activity relationship studies of tryptanthrins as antitubercular agentsJ. Nat. Prod.76(3)354-367(2013) 4.Kawakami, J., Matsushima, N., Ogawa, O., et al.Antibacterial and antifungal activities of tryptanthrin derivativesTrans. Mater. Res. Soc. Jpn.36(4)603-606(2011) 5.Scovill, J., Blank, E., Konnick, M., et al.Antitrypanosomal activities of tryptanthrinsAntimicrob. Agents Chemother.46(3)882-883(2002)

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