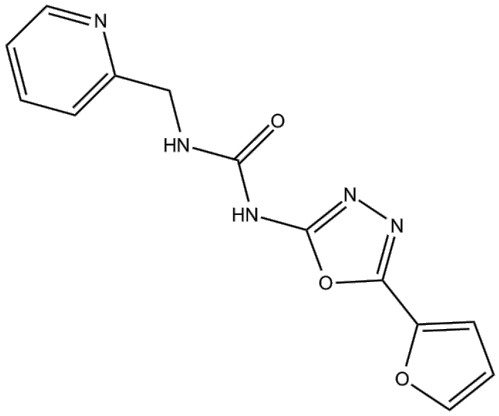
Product Data Sheet

Product Name: NK 252
Cat. No.: GC13058

Chemical Properties

Cas. No.	1414963-82-8		
Chemical Name	N-[5-(2-furanyl)-1,3,4-oxadiazol-2-yl]-N'-(2-pyridinylmethyl)-urea		
SMILES	O=C(NC1=NN=C(C2=CC=CO2)O1)NCC3=CC=CC=N3		
Formula	$C_{13}H_{11}N_5O_3$	M.Wt	285.3
Solubility	≤14mg/ml in DMSO;20mg/ml in dimethyl formamide	Storage	Store at 2-8°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

Product Data Sheet

Cell experiment: The Huh-7.5 cells, a subline derived from Huh-7 cells, are transfected with ARE/pGL4.32 by lipofectamine LTX. The stable clonal transfectant is isolated by selection in hygromycin B (0.1 mg/mL). Cells derived from stable clones are transfected with control or Nrf2 small interfering RNA by lipofectamine RNAiMAX (30 hours), then treated with OPZ, NK-252 (0.1-30 μM, 16 hours) , or DMSO alone (control). The luciferase activity values are measured using the Steady-Glo Luciferase Assay System[1].

Animal experiment: Rats[1]Six-week-old male Fischer 344 rats are randomly divided into four compound administration groups and four control groups. Compound administration groups of rats fed a CDAA diet receive oral administration as follows: 1) OPZ from 1 week after feeding at a dose of 60 mg/kg once daily for 9 weeks (CDAA+OPZ group; N=8), 2) NK-252 from 1 week after feeding at a dose of 20 mg/kg once daily for 9 weeks (CDAA+NK-252_low group; N=8), 3) NK-252 from 1 week after feeding at a dose of 60 mg/kg once daily for 9 weeks (CDAA+NK-252_high group; N=8), or 4) NK-252 from 6 weeks after feeding at a dose of 60 mg/kg once daily for 4 weeks (CDAA+NK-252_delayed administration: DA group; N=7). Two control groups of rats are fed a CDAA diet for 6 or 10 weeks (pre-CDAA control or CDAA control group; N=9 each), and the other two control groups of rats are fed standard rodent chow (CRF-1) for 6 or 10 weeks (prenaive or naive; N=3 each). Laparotomy and blood sampling are performed under isoflurane anesthesia. After blood sampling, rats are euthanized by exsanguination under isoflurane anesthesia, and the livers are immediately extirpated.[2]Mice[2]Six- to 8-week-old male BALB/c x DBA/2 F1 (hereafter called CD2F1) mice weighing 22 to 26 g are used. Male CD2F1 mice are inoculated i.p. with 106 cells of P388/S and P388/VCR cell line on day 0. Each group consist of six mice. NK-250 and NK-252 (100, 300, and 1000 mg/kg) are given p.o. daily from day 1 to 5. Mean survival days and the range of survival days are analysed.

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]. Shimozono R et al. Nrf2 activators attenuate the progression of nonalcoholic steatohepatitis-related fibrosis in a dietary rat model. Mol Pharmacol. 2013 Jul, 84(1):62-70.
[2]. Kiue A, et al. Enhancement of antitumour activity of etoposide by dihydropyridines on drug-sensitive and drug-resistant leukaemia in mice. Br J Cancer. 1991 Aug;64(2):221-6.

Background

NK 252 is an Nrf2 activator [1][2]. Nuclear factor-erythroid-2-related factor 2 (Nrf2), a transcription factor that activates antioxidant response elements (AREs), plays a central role in stimulating the expression of various antioxidant-associated genes in the cellular defense against oxidative stress. Keap1 is a cytosolic repressor of Nrf2 that retains Nrf2 in the cytoplasm [1].

NK 252 is an Nrf2 activator that interacts directly with the domain containing the Nrf2-binding site of Keap1. In Huh-7.5 cells, NK 252 activated the NQO1-ARE in a dose-dependent way, suggesting NK-252 has potential as an Nrf2 activator in hepatic cells. NK-252 also protected Huh-7 cells against H2O2-induced cytotoxicity [1]. NK-252 was effective not only in circumventing drug resistance but also in potentiating the action of antitumor drugs against drug-sensitive tumors [2].

In nonalcoholic steatohepatitis (NASH) model rats, NK-252 decreased fibrosis scores and significantly reduced liver fibrosis area in a dose-dependent way. NK-252 also significantly reduced plasma ALT levels and plasma AST levels, suggesting the hepatoprotective effects of NK-252. NK-252 increased NQO1 gene expression and exhibited antioxidant properties in the livers of rats. NK-252 reduced fibrogenic gene expression and inhibited further progression of established fibrosis [1].

References:
[1]. Shimozono R, Asaoka Y, Yoshizawa Y, et al. Nrf2 activators attenuate the progression of nonalcoholic steatohepatitis-related fibrosis in a dietary rat model. Mol Pharmacol. 2013 Jul;84(1):62-70.
[2]. Kiue A, Sano T, Naito A, et al. Reversal by two dihydropyridine compounds of resistance to multiple anticancer agents in mouse P388 leukemia in vivo and in vitro. Jpn J Cancer Res. 1990 Oct;81(10):1057-64.

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