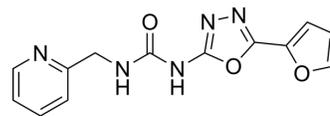


NK-252

Cat. No.:	HY-19734		
CAS No.:	1414963-82-8		
Molecular Formula:	C ₁₃ H ₁₁ N ₅ O ₃		
Molecular Weight:	285.26		
Target:	Keap1-Nrf2		
Pathway:	NF-κB		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 29 mg/mL (101.66 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	3.5056 mL	17.5279 mL	35.0557 mL
	5 mM	0.7011 mL	3.5056 mL	7.0111 mL
	10 mM	0.3506 mL	1.7528 mL	3.5056 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.08 mg/mL (7.29 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.08 mg/mL (7.29 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.08 mg/mL (7.29 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NK-252 is a potential Nrf2 activator, which exhibits a great Nrf2-activating potential.

IC₅₀ & Target

Nrf2^[1]

In Vitro

The luciferase activity in Huh-7.5 cells treated with Oltipraz (OPZ) or NK-252 shows activation of the NAD(P)H quinone oxidoreductase 1 (NQO1)-ARE in a dose-dependent manner. NK-252 displays this effect with higher potency than OPZ based

on the fact that the EC₂ value (concentration for a 2-fold induction above background), calculated with linear extrapolation from the values above and below the induction threshold, is 20.8 μM for OPZ and 1.36 μM for NK-252. NK-252 has potential as an Nrf2 activator in hepatic cells. Prototypical Nrf2 activators that include OPZ have been reported to protect microglial cells from H₂O₂-induced cytotoxicity. The protective effects of OPZ and NK-252 are examined against H₂O₂-induced cytotoxicity using Huh-7 cells to evaluate their antioxidant properties. The cells treated with OPZ or NK-252 show increased resistance to H₂O₂-induced cytotoxicity compared with control cells^[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Rats on a choline-deficient L-amino acid–defined (CDAA) diet given OPZ or NK-252 display decreased fibrosis scores compared with CDAA control rats, with median scores of 3, corresponding to bridging fibrosis. CDAA control rats display approximately 20-fold augmentation of the liver fibrosis area compared with rats fed a normal control diet (naive) (14.7 and 0.72%, respectively). This augmentation is also drastically reduced by administration of OPZ or NK-252 (5.80% for OPZ, 6.20% for NK-252_{low}, and 4.97% for NK-252_{high}). The effects of NK-252 on both fibrosis score and fibrosis area are dose-dependent^[1]. NK-252 alone has no antitumour effect in P388/S- and P388/VCR-mice. The combination therapy of Etoposide with NK-252 administered p.o. significantly increases the life-span of mice inoculated i.p. with P388/S compared with the corresponding therapeutic effects with Etoposide alone. The combination therapy with Etoposide and NK-252 significantly increases the life-span of mice inoculated i.p. with P388/VCR compared with the corresponding survival time with Etoposide alone^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[1]

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^{[1][2]}

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 (pre-naive 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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Metab. 2023 Oct 3;35(10):1688-1703.e10.

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- Cell Death Dis. 2020 Jul 30;11(7):607.
 - Phytomedicine. 2024 Feb 1, 155401.
 - iScience. 2020 Apr.
 - Aging. 2020 Nov 7;12(21):21161-21185.

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REFERENCES

- [1]. Shimozone 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.
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Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA