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产品名称：NK-252
产品别名：NK-252

生物活性：

Description	NK-252 is a potential Nrf2 activator, which exhibits a great Nrf2-activating potential.
IC_{50} & 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 H_2O_2-induced cytotoxicity. The protective effects of OPZ and NK-252 are examined against H_2O_2-induced cytotoxicity using Huh-7 cells to evaluate their antioxidant properties. The cells treated with OPZ or NK-252 show increased resistance to H_2O_2-induced cytotoxicity compared with control cells[1].
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].

In Vitro:

DMSO : ≥ 29 mg/mL (101.66 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

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Solvent&Solubility	——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.08 mg/mL (7.29 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (7.29 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (7.29 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (7.29 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.08 mg/mL (7.29 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (7.29 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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 Administration	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-252from 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 F_1 (hereafter called $CD2F_1$) mice weighing 22 to 26 g are used. Male $CD2F_1$ mice are inoculated i.p. with 10^6 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.
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.