

Product Data Sheet

Product Name: Nintedanib esylate

Cat. No.: GC36745

Chemical Properties

Cas. No. 656247-18-6

SMILES O=C(C1=CC(NC(=O)C(=C1)C2=C(NC3=CC=C(N(C)C(CN4CCN(C)CC4)=O)C=C3)/C5=CC=CC=C5)OC.CCS(=O)(O)=O

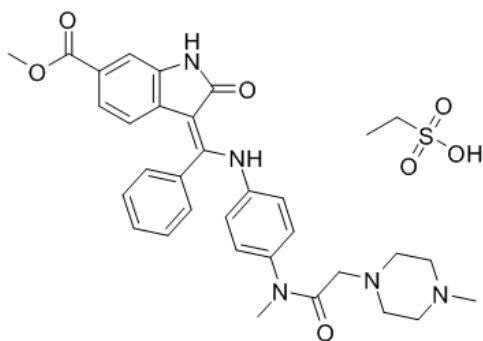
Formula $C_{33}H_{39}N_5O_7S$ M.Wt 649.76

Solubility DMSO: 92.85 mg/mL (142.90 mM and warming) 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 HUVECs

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

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Preparation Method The cell viability was detected after HUVECs were added with Nintedanib (1, 5, 10, 25, 50, and 100 μ M) to determine the optimized incubation concentrations.

Reaction Conditions 1, 5, 10, 25, 50, and 100 μ M; for 24 hours

Applications When the concentration of Nintedanib was greater than 50 μ M, a significantly declined viability of HUVECs was observed.

Animal experiment [2]:

Animal models male TRAMP mice

Preparation Method In pre-clinical efficacy evaluation, male TRAMP mice starting at 8 and 12 weeks of age were orally-fed with vehicle control (10% Tween 20) or Nintedanib (10 mg/Kg/day in vehicle control) for 4 weeks, and sacrificed immediately after 4 weeks of drug treatment or sacrificed 6-10 weeks after stopping drug treatments.

Dosage form 10 mg/Kg/day; p.o.

Applications In pre-clinical TRAMP studies, Nintedanib led to a delay in tumor progression in all treatment groups; the effect was more pronounced when treatment was given at the beginning of the glandular lesion development and continued till study end.

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Li L, et al. Nintedanib ameliorates oxidized low-density lipoprotein -induced inflammation and cellular senescence in vascular endothelial cells. Bioengineered. 2022 Mar;13(3):6196-6207.

da Silva RF, et al. Nintedanib antiangiogenic inhibitor effectiveness in delaying adenocarcinoma progression in Transgenic Adenocarcinoma of the Mouse Prostate (TRAMP). J Biomed Sci. 2017 May 12;24(1):31.

Background

Nintedanib esylate, as a kinase inhibitor, used for the treatment of non-small cell lung cancer suffered from first-pass metabolism which resulted in low oral bioavailability (~ 4.7%)^[1]. Nintedanib is an effective inhibitor of multityrosine kinase receptors.

In vitro, treatment with 1-4 μ M nintedanib in a dose-dependently manner in Keloid fibroblasts inhibited cell proliferation, induced G0/G1 cell cycle arrest, and suppressed migration and invasion of keloid fibroblasts^[2]. In vitro test it shown that at 1 μ M Nintedanib and 2.5 mM Pirfenidone decreased fibrotic gene expression including Collagen 1a1 and Fibronectin in murine and human 3D-LTCs as well as pmATII cells^[3]. In vitro, 0.01-1.0 μ M nintedanib in IPF (Idiopathic pulmonary fibrosis) fibroblasts decreased the expression of collagen I and V, fibronectin, and FKBP10 and attenuated the secretion of collagen I and III^[4].

In vivo efficacy test it exhibited that treatment with 5 mg/mL nintedanib in eye drops four times daily, the outgrowths of blood and lymphatic vessels were obviously inhibited compared with the controls^[5]. In vivo, treatment with 3 μ M and 5 μ M nintedanib in mice up-regulated SP-D (Pulmonary surfactant protein D) messenger RNA expression^[6]. In vivo experiment it demonstrated that treatment with nintedanib (50, 100 mg/kg) orally could obviously recover the experimental colitis-related symptoms of mice caused by DSS, such as weight loss, increased DAI, shortened colon length, and colonic tissue injury^[7].

Kala SG, et al. Bioavailability enhancement of vitamin E TPGS liposomes of nintedanib esylate: formulation optimization, cytotoxicity and pharmacokinetic studies. Drug Deliv Transl Res. 2022 Nov;12(11):2856-2864.

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Lehmann M, et al. Differential effects of Nintedanib and Pirfenidone on lung alveolar epithelial cell function in ex vivo murine and human lung tissue cultures of pulmonary fibrosis. Respir Res. 2018 Sep 15;19(1):175.

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Lin T, et al. Inhibition of lymphangiogenesis in vitro and in vivo by the multikinase inhibitor nintedanib. Drug Des Devel Ther. 2017 Apr 5;11:1147-1158.

Kamio K, et al. Nintedanib modulates surfactant protein-D expression in A549 human lung epithelial cells via the c-Jun N-terminal kinase-activator protein-1 pathway. Pulm Pharmacol Ther. 2015 Jun;32:29-36.

Li H, et al. Nintedanib Alleviates Experimental Colitis by Inhibiting CEBPB/PCK1 and CEBPB/EFNA1 Pathways. Front Pharmacol. 2022 Jul 14;13:904420.

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