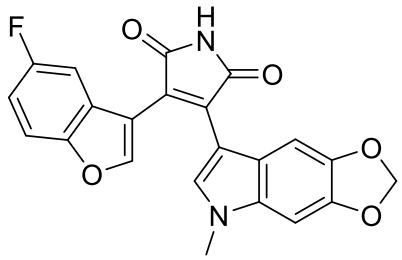
Product data sheet

MedKoo Cat#: 562032 Name: 9-ING-41 CAS#: 1034895-42-5 Chemical Formula: $C_{22}H_{13}FN_2O_5$ Exact Mass: 404.0808 Molecular Weight: 404.35	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

9-ING-41 is a glycogen synthase kinase-3 (GSK-3) inhibitor. 9-ING-41 leads to cell cycle arrest, autophagy and apoptosis in bladder cancer cells. 9-ING-41 enhanced the growth inhibitory effects of gemcitabine or cisplatin when used in combination in bladder cancer cells. 9-ING-41 sensitized bladder cancer cells to the cytotoxic effects of human immune effector cells.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	5.0	12.37

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.47 mL	12.37 mL	24.73 mL
5 mM	0.49 mL	2.47 mL	4.95 mL
10 mM	0.25 mL	1.24 mL	2.47 mL
50 mM	0.05 mL	0.25 mL	0.49 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Karmali R, Chukkapalli V, Gordon LI, Borgia JA, Ugolkov A, Mazar AP, Giles FJ. GSK-3β inhibitor, 9-ING-41, reduces cell viability and halts proliferation of B-cell lymphoma cell lines as a single agent and in combination with novel agents. Oncotarget. 2017 Nov 11;8(70):114924-114934. doi: 10.18632/oncotarget.22414. PMID: 29383130; PMCID: PMC5777742.
2. Kuroki H, Anraku T, Kazama A, Bilim V, Tasaki M, Schmitt D, Mazar AP, Giles FJ, Ugolkov A, Tomita Y. 9-ING-41, a small molecule inhibitor of GSK-3beta, potentiates the effects of anticancer therapeutics in bladder cancer. Sci Rep. 2019 Dec 27;9(1):19977. doi: 10.1038/s41598-019-56461-4. PMID: 31882719; PMCID: PMC6934761.

In vivo study

1.Ugolkov AV, Bondarenko GI, Dubrovskyi O, Berbegall AP, Navarro S, Noguera R, O'Halloran TV, Hendrix MJ, Giles FJ, Mazar AP. 9-ING-41, a small-molecule glycogen synthase kinase-3 inhibitor, is active in neuroblastoma. Anticancer Drugs. 2018 Sep;29(8):717-724. doi: 10.1097/CAD.0000000000000652. PMID: 29846250; PMCID: PMC6092218.
2. Jeffers A, Qin W, Owens S, Koenig KB, Komatsu S, Giles FJ, Schmitt DM, Idell S, Tucker TA. Glycogen Synthase Kinase-3β Inhibition with 9-ING-41 Attenuates the Progression of Pulmonary Fibrosis. Sci Rep. 2019 Dec 12;9(1):18925. doi: 10.1038/s41598-019-55176-w. PMID: 31831767; PMCID: PMC6908609.

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7. Bioactivity

Biological target:

9-ING-41 is a maleimide-based ATP-competitive and selective glycogen synthase kinase-3β (GSK-3β) inhibitor with an IC50 of 0.71 μM.

In vitro activity

9-ING-41 was tested in T24, HT1376 and RT4 bladder cancer cell lines. 9-ING-41 treatment resulted in a decreased growth of bladder cancer cells at 0.25–1 μM concentrations in a dose-dependent manner with GI50 range of 0.4–0.5 μM (Fig. 1A). Moreover,a cytotoxic effect of 9-ING-41 was found in RT4 bladder cancer cells at >0.5 μM concentrations of 9-ING-41 (Fig. 1A). Cell cycle blockage was found at G2/M after 24 hours of 9-ING-41 treatment (Fig. 1C), suggesting that GSK-3 inactivation by 9-ING-41 halts progression of mitosis in bladder cancer cells. To investigate the mechanistic effect of GSK-3 inhibitor 9-ING-41 in the blockage of cell cycle in bladder cancer cells, the expression of G2/M regulatory proteins Cdk1 and Cyclin B1 was examined in 9-ING-41-treated cells. It was found that expression of Cdk1 and Cyclin B1 proteins was significantly decreased in 9-ING-41-treated bladder cancer cells (Fig. 2A). Moreover, treatment with 9-ING-41 led to a decreased expression of antiapoptotic molecules, Bcl-2 and XIAP, resulted in an increased apoptosis as shown by PARP cleavage in bladder cancer cells (Fig. 2A,B). Furthermore, caspase activation assay was used to demonstrate that 9-ING-41 treatment induces apoptotic cell death in bladder cancer cells (Fig. 2C). These in vitro results suggest that treatment with GSK-3 inhibitor 9-ING-41 suppresses expression of G2/M regulatory proteins and antiapoptotic molecules leading to cell cycle arrest and apoptosis in bladder cancer cells, and identify 9-ING-41 as a candidate for the targeted therapy of human bladder cancer.

Reference: Sci Rep. 2019; 9: 19977. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6934761/

In vivo activity

In these studies, 9-ING-41 treatment was initiated 7 days after instillation of the adenoviral vectors. 9-ING-41 significantly improved decrements ($p < 0.05$) in lung compliance and lung volume compared to TGF-β adenoviral treated mice (Fig. 6A). Lung injury by morphometry was next analyzed using a 3-point scale, where 1 = no scarring and 3 = extensive scarring. 9-ING-41 treatment significantly reduced the lung injury score of TGF-β adenovirus induced PF in mice (Fig. 6B, $p = 0.02$). Collagen deposition (Fig. 6C) was likewise significantly reduced by 9-ING-41 treatment (Fig. 6C, $p = 0.03$). TGF-β adenovirus treated mice also demonstrated significantly increased numbers of apoptotic cells compared to GFP adenovirus controls. 9-ING-41 treatment significantly reduced the number of apoptotic cells, presumably including alveolar epithelial cells, in TGF-β treated mice compared to GFP adenoviral controls (Fig. 6D). While DMSO treated mice showed pronounced injury and areas of intense collagen deposition, 9-ING-41 treated mice had significantly fewer areas of injury and demonstrated less collagen deposition (Fig. 7B). These findings strongly support the hypothesis that the therapeutic targeting of GSK-3β with the novel inhibitor, 9-ING-41, reduces myofibroblast differentiation, collagen deposition, and subsequent PF in vivo.

Reference: Sci Rep. 2019; 9: 18925. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6908609/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.