# Product data sheet

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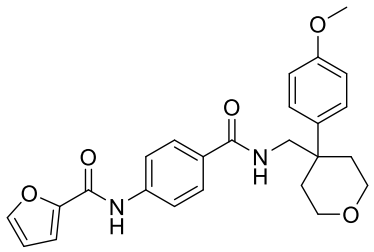
|---|---|
| MedKoo Cat#: 406502<br>Name: JW55<br>CAS#: 664993-53-7<br>Chemical Formula: $C_{25}H_{26}N_2O_5$<br>Exact Mass: 434.18417<br>Molecular Weight: 434.48434 |  |
| Product supplied as: | Powder |
| Purity (by HPLC): | ≥ 98% |
| Shipping conditions | Ambient temperature |
| Storage conditions: | Powder: -20°C 3 years; 4°C 2 years. |
| | In solvent: -80°C 3 months; -20°C 2 weeks. |

**1. Product description:**
JW55 is a tankyrase 1 and tankyrase 2 (TNKS1/2) inhibitor. JW55 functions via inhibition of the PARP domain of tankyrase 1 and tankyrase 2 (TNKS1/2), regulators of the β-catenin destruction complex. Inhibition of TNKS1/2 poly(ADP-ribosyl)ation activity by JW55 led to stabilization of AXIN2, a member of the β-catenin destruction complex, followed by increased degradation of β-catenin. In a dose-dependent manner, JW55 inhibited canonical Wnt signaling in colon carcinoma cells that contained mutations in either the APC (adenomatous polyposis coli) locus or in an allele of β-catenin. In addition, JW55 reduced XWnt8-induced axis duplication in Xenopus embryos and tamoxifen-induced polyposis formation in conditional APC mutant mice.

**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 | 50 | 115.08 |

**4. Stock solution preparation table:**

| Concentration / Solvent Volume / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 2.30 mL | 11.51 mL | 23.02 mL |
| 5 mM | 0.46 mL | 2.30 mL | 4.60 mL |
| 10 mM | 0.23 mL | 1.15 mL | 2.30 mL |
| 50 mM | 0.05 mL | 0.23 mL | 0.46 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. Waaler J, Machon O, Tumova L, Dinh H, Korinek V, Wilson SR, Paulsen JE, Pedersen NM, Eide TJ, Machonova O, Gradl D, Voronkov A, von Kries JP, Krauss S. A novel tankyrase inhibitor decreases canonical Wnt signaling in colon carcinoma cells and reduces tumor growth in conditional APC mutant mice. Cancer Res. 2012 Jun 1;72(11):2822-32. doi: 10.1158/0008-5472.CAN-11-3336. Epub 2012 Mar 22. PMID: 22440753.

In vivo study

1. Waaler J, Machon O, Tumova L, Dinh H, Korinek V, Wilson SR, Paulsen JE, Pedersen NM, Eide TJ, Machonova O, Gradl D, Voronkov A, von Kries JP, Krauss S. A novel tankyrase inhibitor decreases canonical Wnt signaling in colon carcinoma cells and reduces tumor growth in conditional APC mutant mice. Cancer Res. 2012 Jun 1;72(11):2822-32. doi: 10.1158/0008-5472.CAN-11-3336. Epub 2012 Mar 22. PMID: 22440753.

**7. Bioactivity**
Biological target:

# Product data sheet

JW 55 is a potent and selective β-catenin signaling pathway inhibitor, which functions via inhibition of the PARP domain of tankyrase 1 and tankyrase 2 (TNKS1/2).

## In vitro activity

The cell lines SW480 and HCT-15 (mutated in codon 1338 and 1417 of the APC gene, respectively) were stably transfected with ST-Luc and Renilla and incubated at various doses of JW55 for 48 hours. A dose-dependent reduction of luciferase activity was detected in both cell lines. JW55 was effective in the range of 1 to 5 μmol/L in SW480 cells and 0.01 to 5 μmol/L in HCT-15 cells (Fig. 2B, left). Next, HCT116 CRC cells with integrated ST-Luc and Renilla reporters were used to test JW55. HCT116 carries a point mutation in the CK1α-dependent phosphorylation site S45 of one β-catenin allele; however, S45-mutated β-catenin may still be phosphorylated in the remaining GSK3β phosphorylation sites (e.g. S33, S37, and T41), with resulting semiregulated β-catenin turnover. In HCT116 cells, JW55 was effective in the range of 0.01 to 5 μmol/L (Fig. 2B, right). A basal luciferase expression level at approximately 50% was reached after exposure to 5 μmol/L in the CRC cells.

Reference: Cancer Res. 2012 Jun 1;72(11):2822-32. http://cancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=22440753

## In vivo activity

To evaluate the JW55-mediated decrease of intestinal tumor development in vivo, ApcCKO/CKOLgr5-CreERT2+ mice were injected intraperitoneally with a 25 mg/kg single dose of tamoxifen. A day after, daily per oral applications of JW55 (100 mg/kg; 3 females) or vehicle (DMSO; 4 females) were initiated. The dose of 100 mg/kg was chosen to counteract the rapid liver metabolism of JW55 as indicated by the human liver microsome stability analysis (t½ = 10.1 minutes; Supplementary Fig. S7A). No measurable effects on mouse body weight were noticed throughout the experiment period (Supplementary Fig. S7B). After 21 days, the mice were sacrificed and the dissected intestines were embedded in paraffin and sectioned. Immunohistochemical staining revealed that the neoplastic lesions expressed β-catenin and the mouse ISC marker Ephrin type-B receptor 2 (EphB2), indicating aberrant activation of canonical Wnt signaling in the tumor tissue (Fig. 7B; refs. 44, 48–50). The β-catenin–stained colon adenomas contrasted with the surrounding healthy mucosa, and image analysis software (Ellipse) was used to quantify the number and areas of β-catenin–positive lesions in the colon (Supplementary Fig. S7C). As it was impossible to distinguish the borders of individual tumors in the small intestine (ileum), only the total tumor area per mouse was recorded. In the ileum, a significant reduction of the total tumor area was observed after JW55 injections (mean: 2.93 mm2 and median: 2.95 mm2) when compared with the control group (mean: 8.84 mm2 and median: 9.51 mm2; normality test failed, rank sum test: P = 0.003; Fig. 7A and C, top panel). In the colon, the tumor count was substantially reduced in JW55-treated mice (mean: 9.7 and median: 6.0) when evaluated against the control group (mean: 33.8 and median: 26.0; normality test failed, rank sum test: P = 0.057; Fig. 7C, bottom panel). Furthermore, a significant decrease of the total tumor area was noticed after injections with JW55 (mean: 0.022 mm2) when compared with the control group (mean: 0.154 mm2; Students t test: P = 0.009; Fig. 7C, bottom panel). The area of single tumors was significantly reduced after injections with JW55 (mean: 0.0025 mm2) when compared with the untreated group (mean: 0.0049 mm2; Students t test: P = 0.043; Fig. 7C, bottom panel). Interestingly, the proportion of cells that expressed Ki67, a marker of proliferating and ISC-like cells, was substantially decreased in adenomas exposed to JW55 when compared with tumors that developed in the control mice (Fig. 7B, panel h and i).

Reference: Cancer Res. 2012 Jun 1;72(11):2822-32. http://cancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=22440753