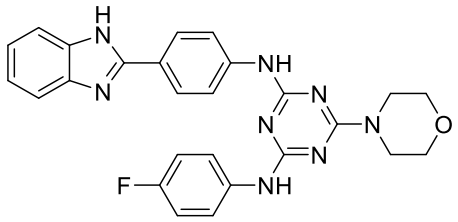
Product data sheet

MedKoo Cat#: 407993 Name: IITZ-01 CAS#: 1807988-47-1 Chemical Formula: $C_{26}H_{23}FN_8O$ Exact Mass: 482.1979 Molecular Weight: 482.5234	
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:
IITZ-01 (Autophagy inhibitor IITZ-01) is a novel potent lysosomotropic autophagy inhibitor. IITZ-01 enhances autophagosome accumulation but inhibit autophagosomal degradation by impairing lysosomal function, finally resulting in the inhibition of autophagy. IITZ-01 exhibited more than 10-fold potent autophagy inhibition along with 12- to 20-fold better cytotoxic action than CQ. IITZ-01 is potent autophagy inhibitor with single-agent anticancer activity and awaits further preclinical development as potential anticancer therapeutic.

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	100	207.24

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.07 mL	10.36 mL	20.72 mL
5 mM	0.41 mL	2.07 mL	4.14 mL
10 mM	0.21 mL	1.04 mL	2.07 mL
50 mM	0.04 mL	0.21 mL	0.41 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. Shahriyar SA, Seo SU, Min KJ, Kubatka P, Min DS, Chang JS, Kim DE, Woo SM, Kwon TK. Upregulation of DR5 and Downregulation of Survivin by IITZ-01, Lysosomotropic Autophagy Inhibitor, Potentiates TRAIL-Mediated Apoptosis in Renal Cancer Cells via Ubiquitin-Proteasome Pathway. Cancers (Basel). 2020 Aug 21;12(9):2363. doi: 10.3390/cancers12092363. PMID: 32825566; PMCID: PMC7564912.

2. Guntuku L, Gangasani JK, Thummuri D, Borkar RM, Manavathi B, Ragampeta S, Vaidya JR, Sistla R, Vegi NGM. IITZ-01, a novel potent lysosomotropic autophagy inhibitor, has single-agent antitumor efficacy in triple-negative breast cancer in vitro and in vivo. Oncogene. 2019 Jan;38(4):581-595. doi: 10.1038/s41388-018-0446-2. Epub 2018 Aug 30. PMID: 30166591.

In vivo study

1. Guntuku L, Gangasani JK, Thummuri D, Borkar RM, Manavathi B, Ragampeta S, Vaidya JR, Sistla R, Vegi NGM. IITZ-01, a novel potent lysosomotropic autophagy inhibitor, has single-agent antitumor efficacy in triple-negative breast cancer in vitro and in vivo. Oncogene. 2019 Jan;38(4):581-595. doi: 10.1038/s41388-018-0446-2. Epub 2018 Aug 30. PMID: 30166591.

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7. Bioactivity

Biological target:

IITZ-01 is a potent lysosomotropic autophagy inhibitor with single-agent antitumor activity, with an IC50 of 2.62 μM for PI3Kγ.

In vitro activity

Sub-lethal concentrations of a lysosomotropic autophagy inhibitor, IITZ-01, sensitizes cancer cells (renal, lung, and breast carcinoma) to TRAIL-induced apoptosis through DR5 upregulation and survivin downregulation through ubiquitin-proteasome pathway. Knockdown of DR5 or overexpression of survivin inhibited combined treatment with IITZ-01 and TRAIL-induced apoptosis. IITZ-01 downregulated protein expression of Cbl, ubiquitin E3 ligase, and decreased expression level of Cbl markedly led to increase DR5 protein expression and TRAIL sensitivity. Moreover, IITZ-01 decreased expression level of survivin protein via downregulation of deubiquitinase ubiquitin-specific protease 9X (USP9X) expression. Taken together, these results provide the first evidence that IITZ-01 enhances TRAIL-mediated apoptosis through DR5 stabilization by downregulation of Cbl and USP9X-dependent survivin ubiquitination and degradation in renal carcinoma cells.

Reference: Cancers (Basel). 2020 Aug 21;12(9):2363. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32825566/

In vivo activity

The antitumor efficacy of IITZ-01 was investigated in in-vivo breast cancer model. MDA-MB-231/green fluorescent protein (GFP) orthotropic breast cancer xenografts were developed in CrTac:NCr-Foxnnu BALB/c female nude mice. Tumors after reaching ~100 mm3, vehicle, 45 mg/kg of IITZ-02, were administered through intraperitoneal (i.p.) route on every alternate day for 4 weeks. IITZ-01 reduced the active tumor burden around 8.8-fold when compared with control group as determined by tumor photon counts. Moreover, tumor volume measurements have demonstrated that IITZ-01 significantly inhibited average tumor growth when compared with control from third day of treatment (Fig. 7a–c). Significant reduction in average tumor weights was observed after treatment with test compounds compared with control (Fig. 7d). This treatment schedule of both compounds was well tolerated in mice for the total duration of administration with no significant changes in their body weights (Fig. 7e). In addition, hematoxylin and eosin staining revealed large areas of necrosis in treated groups of both compounds when compared with controls. Immunohistochemistry in histological sections revealed that exposure of both compounds have enhanced LC3-II- and PARP-positive staining in cells than vehicle control, indicating effective autophagy inhibition and triggering of apoptosis (Fig. 7f). Altogether, these findings demonstrated that IITZ-01 inhibits breast tumor growth by autophagy inhibition and apoptosis induction in vivo.

Reference: Oncogene. 2019 Jan;38(4):581-595. https://doi.org/10.1038/s41388-018-0446-2

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.