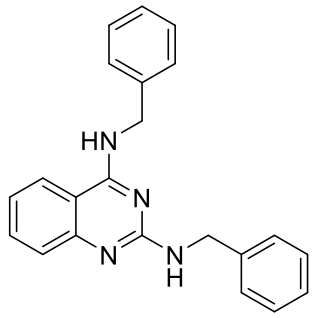
Product data sheet

MedKoo Cat#: 406758 Name: DBeQ CAS#: 177355-84-9 Chemical Formula: $C_{22}H_{20}N_4$ Exact Mass: 340.1688 Molecular Weight: 340.43	
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:

DBeQ, also known as JRF 12, is a selective, reversible, and ATP-competitive inhibitor of the ATPase p97 for treatment of cancer. DBeQ impairs both ubiquitin-dependent and autophagic protein clearance pathways. DBeQ was shown to inhibit the ATPase activity of Vps4 with an IC50 of about 11.5 μM. To a less degree, it also inhibits hyphal growth. DBeQ blocks multiple processes that have been shown by RNAi to depend on p97, including degradation of ubiquitin fusion degradation and endoplasmic reticulum-associated degradation pathway reporters, as well as autophagosome maturation. DBeQ also potently inhibits cancer cell growth and is more rapid than a proteasome inhibitor at mobilizing the executioner caspases-3 and -7.

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	41.0	120.44
Ethanol	3.2	9.40

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.94 mL	14.69 mL	29.37 mL
5 mM	0.59 mL	2.94 mL	5.87 mL
10 mM	0.29 mL	1.47 mL	2.94 mL
50 mM	0.06 mL	0.29 mL	0.59 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. Chou TF, Brown SJ, Minond D, Nordin BE, Li K, Jones AC, Chase P, Porubsky PR, Stoltz BM, Schoenen FJ, Patricelli MP, Hodder P, Rosen H, Deshaies RJ. Reversible inhibitor of p97, DBeQ, impairs both ubiquitin-dependent and autophagic protein clearance pathways. Proc Natl Acad Sci U S A. 2011 Mar 22;108(12):4834-9. doi: 10.1073/pnas.1015312108. Epub 2011 Mar 7. PMID: 21383145; PMCID: PMC3064330.

2. Nabhan JF, Gooch RL, Piatnitski Chekler EL, Pierce B, Bulawa CE. Perturbation of cellular proteostasis networks identifies pathways that modulate precursor and intermediate but not mature levels of frataxin. Sci Rep. 2015 Dec 16;5:18251. doi: 10.1038/srep18251. PMID: 26671574; PMCID: PMC4680912.

In vivo study

1. Zhang Z, Wang Y, Li C, Shi Z, Hao Q, Wang W, Song X, Zhao Y, Jiao S, Zhou Z. The Transitional Endoplasmic Reticulum ATPase p97 Regulates the Alternative Nuclear Factor NF-κB Signaling via Partial Degradation of the NF-κB Subunit p100. J Biol Chem. 2015 Aug 7;290(32):19558-68. doi: 10.1074/jbc.M114.630061. Epub 2015 Jun 25. PMID: 26112410; PMCID: PMC4528123.

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7. Bioactivity

Biological target:

DBeQ is a selective, potent, reversible, and ATP-competitive p97 inhibitor, with an IC50 value of 1.5 μM and 1.6 μM for p97(wt) and p97(C522A), respectively; DBeQ also inhibits Vps4 with an IC50 of 11.5 μM.

In vitro activity

10 μM DBeQ rapidly promoted activation of the "executioner" caspases-3 and -7 in HeLa cells (Fig. 4A). DBeQ was benchmarked by comparing it with the well-characterized apoptosis inducer staurosporine (STS) and the procaspases-3 and -6 activator 1541. STS induces executioner caspases-3, -6, and -7 via both caspases-8 and -9 in the apoptotic pathway. DBeQ activated caspases-3 and -7 by twofold within 2 h (Fig. 4B) but did not activate caspase-6 after 6 h (Fig. 4C). The impact of DBeQ on initiator caspases-8 and -9 was next evaluated. DBeQ activated the intrinsic caspase-9 apoptotic pathway more than the extrinsic caspase-8 pathway, whereas STS activated both pathways to a similar extent (Fig. 4 D and E). DBeQ was blocked by the general caspase inhibitor [Z-VAD(OMe)FMK; Fig. 4G], whereas accumulation of LC3-II was not affected (Fig. 3D, lane 3), suggesting that the block in autophagosome maturation induced by DBeQ was not an indirect consequence of caspase activation. DBeQ potently inhibits cancer cell growth and is more rapid than a proteasome inhibitor at mobilizing the executioner caspases-3 and -7. The results provide a rationale for targeting p97 in cancer therapy.

Reference: Proc Natl Acad Sci U S A. 2011 Mar 22; 108(12): 4834–4839. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3064330/

In vivo activity

To further corroborate our mechanistic study of p97 regulation of the p100 processing, we developed LPS-induced lung pathology model in mock mice and p97-KD mice by intraperitoneal injection of LPS (20 mg/kg) every day (Fig. 5A). As shown in Fig. 5D, DBeQ treatment substantially blocked the processing of p100 into p52, again supporting the notion that p97 facilitates the partial degradation of p100. Consistently, such catalytic inhibition of p97 dramatically down-regulated the transcription of NFKB2 (Fig. 5E).

Reference: J Biol Chem. 2015 Aug 7; 290(32): 19558–19568. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4528123/

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.